Clinical trial results:
A phase III, randomized, open, controlled, multicenter primary vaccination study to demonstrate the non inferiority of the immunogenicity of meningococcal vaccine GSK134612 given intramuscularly versus Mencevax™ ACWY given subcutaneously to healthy subjects aged 11 through 17 years

Summary

EudraCT number	2012-000282-20
Trial protocol	Outside EU/EEA
Global end of trial date	10 September 2008

Results information

Result version number	v2
This version publication date	10 August 2016
First version publication date	06 March 2015
Version creation reason	• Correction of full data set Data (typos) were corrected.

Trial information

Trial identification

Sponsor protocol code	109069

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00464815
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, 1330
Public contact	Clinical Disclosure Advisor, GlaxoSmithKline Biologicals, +44 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Disclosure Advisor, 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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	24 April 2009
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 April 2008
Global end of trial reached?	Yes
Global end of trial date	10 September 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

One month after vaccination:
- To demonstrate the non-inferiority of the vaccine response induced by meningococcal vaccine GSK134612 compared to the licensed Mencevax ACWY measured by serum bactericidal antibodies using baby rabbit complement.
- To demonstrate the non-inferiority of meningococcal vaccine GSK 134612 compared to the licensed Mencevax ACWY in terms of the incidence of any grade 3 systemic symptom within four days after vaccination based on the analysis of pooled safety and reactogenicity data of this present study and study 109067 (MenACWY-TT-035).

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	02 May 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	India: 398
Country: Number of subjects enrolled	Philippines: 392
Country: Number of subjects enrolled	Taiwan: 235
Worldwide total number of subjects	1025
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)	172
Adolescents (12-17 years)	853
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was planned to enrol 1024 healthy male and female subjects in India, Philippines and Taiwan from February 2007 to August 2007.

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	1025
Number of subjects completed	1025

Period 1

Period 1 title	Overall (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 meningococcal vaccine Nimenrix

Arm type	Experimental
Investigational medicinal product name	Nimenrix
Investigational medicinal product code	GSK134612
Other name	Meningococcal serogroups A, C, W-135, Y tetanus toxoid conjugate vaccine
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose by intramuscular injection in the deltoid region of the non-dominant arm

Arm title	Mencevax ACWY Group

Arm description:

Subjects received 1 dose of Mencevax™ ACWY vaccine

Arm type	Active comparator
Investigational medicinal product name	Mencevax ACWY
Investigational medicinal product code	
Other name	Meningococcal serogroups A, C, W-135, Y plain polysaccharide vaccine
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1 dose subcutaneously in the non-dominant upper arm

Number of subjects in period 1	Nimenrix Group	Mencevax ACWY Group
Started	768	257
Completed	762	254
Not completed	6	3
Consent withdrawn by subject	6	3

Baseline characteristics

Reporting groups	
Reporting group title	Nimenrix Group
Reporting group description:	
Subjects received 1 dose of meningococcal vaccine Nimenrix	
Reporting group title	Mencevax ACWY Group
Reporting group description:	
Subjects received 1 dose of Mencevax™ ACWY vaccine	

Reporting group values	Nimenrix Group	Mencevax ACWY Group	Total
Number of subjects	768	257	1025
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			
Healthy males and females aged 11 through 17 years who previously completed routine childhood immunizations to the best of parents'/guardians'knowledge and whose parents/guardians gave written informed consent. No previous vaccination with meningoccal polysaccharide vaccine of serogroups A, C, W-135 and/or Y within the last 5 years, or with meningococcal polysaccharide conjugate vaccine of serogroups A, C, W-135 and/or Y since birth. No previous vaccination with tetanus toxoid within the last month			
Units: years			
arithmetic mean	14.3	14.3	
standard deviation	± 1.97	± 1.97	-
Gender categorical Units: Subjects			
Female	414	135	549
Male	354	122	476

Subject analysis sets	
Subject analysis set title	Nimenrix Group (without subjects of excluded center)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects from the Nimenrix Group who had no GCP issues .	
Subject analysis set title	Mencevax ACWY Group (without subjects of the excluded center)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects from the Mencevax ACWY Group who had no GCP issues.	

Subject analysis set title	109067 Nimenrix Group
Subject analysis set type	Safety analysis
Subject analysis set description: Nimenrix Group from study MenACWY-TT-035 (109067).	
Subject analysis set title	109067 Mencevax Group
Subject analysis set type	Safety analysis
Subject analysis set description: Mencevax Group from study MenACWY-TT-035 (109067).	

Reporting group values	Nimenrix Group (without subjects of excluded center)	Mencevax ACWY Group (without subjects of the excluded center)	109067 Nimenrix Group
Number of subjects	474	159	935
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			
Healthy males and females aged 11 through 17 years who previously completed routine childhood immunizations to the best of parents'/guardians'knowledge and whose parents/guardians gave written informed consent. No previous vaccination with meningoccal polysaccharide vaccine of serogroups A, C, W-135 and/or Y within the last 5 years, or with meningococcal polysaccharide conjugate vaccine of serogroups A, C, W-135 and/or Y since birth. No previous vaccination with tetanus toxoid within the last month			
Units: years arithmetic mean standard deviation	 14.5 ± 1.92	 14.5 ± 1.93	 ±
Gender categorical Units: Subjects			
Female Male	257 217	84 75	

Reporting group values	109067 Mencevax Group		
Number of subjects	312		
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			
Healthy males and females aged 11 through 17 years who previously completed routine childhood immunizations to the best of parents'/guardians'knowledge and whose parents/guardians gave written informed consent. No previous vaccination with meningoccal polysaccharide vaccine of serogroups A, C, W-135 and/or Y within the last 5 years, or with meningococcal polysaccharide conjugate vaccine of serogroups A, C, W-135 and/or Y since birth. No previous vaccination with tetanus toxoid within the last month			
Units: years arithmetic mean standard deviation	±		
Gender categorical Units: Subjects			
Female Male			

End points

End points reporting groups

Reporting group title	Nimenrix Group
Reporting group description: Subjects received 1 dose of meningococcal vaccine Nimenrix	
Reporting group title	Mencevax ACWY Group
Reporting group description: Subjects received 1 dose of Mencevax™ ACWY vaccine	
Subject analysis set title	Nimenrix Group (without subjects of excluded center)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subjects from the Nimenrix Group who had no GCP issues .	
Subject analysis set title	Mencevax ACWY Group (without subjects of the excluded center)
Subject analysis set type	Sub-group analysis
Subject analysis set description: Subjects from the Mencevax ACWY Group who had no GCP issues.	
Subject analysis set title	109067 Nimenrix Group
Subject analysis set type	Safety analysis
Subject analysis set description: Nimenrix Group from study MenACWY-TT-035 (109067).	
Subject analysis set title	109067 Mencevax Group
Subject analysis set type	Safety analysis
Subject analysis set description: Mencevax Group from study MenACWY-TT-035 (109067).	

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

End point title	Number of subjects with a vaccine response to MenA, MenC, MenY and MenW-135
End point description:	
End point type	Primary
End point timeframe: One month after vaccination	

End point values	Nimenrix Group	Mencevax ACWY Group	Nimenrix Group (without subjects of excluded center)	Mencevax ACWY Group (without subjects of the excluded center)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	657	219	378	127
Units: Subjects				
rSBA-MenA (N=553,191,314,108)	472	148	273	84
rSBA-MenC (N=642,211,365,119)	625	204	350	115
rSBA-MenW-135 (N=639,216,362,125)	616	189	350	115
rSBA-MenY (N=657,219,378,127)	616	172	359	100

Statistical analyses

Statistical analysis title	Difference in % subjects with rSBA-MenA response

Statistical analysis description:

To demonstrate the non-inferiority of Nimenrix vaccine versus Mencevax ACWY vaccine in term of rSBA vaccine response, the standardized asymptotic 95% CI for the difference in rSBA vaccine response rate for each of the meningococcal serogroups (Nimenrix Group rate minus Mencevax ACWY Group rate) one month after vaccination was computed.

Comparison groups	Nimenrix Group v Mencevax ACWY Group
Number of subjects included in analysis	876
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Rate difference
Point estimate	7.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.63
upper limit	14.87

Notes:

[1] - Criterion for non-inferiority: the lower limit of the 2-sided standardized asymptotic 95% confidence interval for the group difference (Nimenrig Group minus Mencevax ACWY Group) in the percentage of subjects with bactericidal vaccine response was greater than or equal to the pre-defined clinical limit of -10%

Statistical analysis title	Difference in % subjects with rSBA-MenC response

Statistical analysis description:

To demonstrate the non-inferiority of NImenriv vaccine versus Mencevax ACWY vaccine in term of rSBA vaccine response, the standardized asymptotic 95% CI for the difference in rSBA vaccine response rate for each of the meningococcal serogroups (Nimenrix Group rate minus Mencevax ACWY Group rate) one month after vaccination was computed.

Comparison groups	Nimenrix Group v Mencevax ACWY Group
Number of subjects included in analysis	876
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Rates Difference
Point estimate	0.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.65
upper limit	4.18

Notes:

[2] - Criterion for non-inferiority: the lower limit of the 2-sided standardized asymptotic 95% confidence interval for the group difference [Nimenrix Group minus Mencevax ACWY Group] in the percentage of subjects with bactericidal vaccine response was greater than or equal to the pre-defined clinical limit of -10%

Statistical analysis title	Difference in % subjects with rSBA-MenW135response

Statistical analysis description:

To demonstrate the non-inferiority of Nimenrix vaccine versus Mencevax ACWY vaccine in term of rSBA vaccine response, the standardized asymptotic 95% CI for the difference in rSBA vaccine response rate for each of the meningococcal serogroups (Nimenrix Group rate minus Mencevax ACWY Group rate) one month after vaccination was computed.

Comparison groups	Mencevax ACWY Group v Nimenrix Group
Number of subjects included in analysis	876
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Rate difference
Point estimate	8.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.78
upper limit	14.14

Notes:

[3] - Criterion for non-inferiority: the lower limit of the 2-sided standardized asymptotic 95% confidence interval for the group difference [Nimenrix Group minus Mencevax ACWY Group] in the percentage of subjects with bactericidal vaccine response was greater than or equal to the pre-defined clinical limit of -10%

Statistical analysis title	Difference in % subjects with rSBA-MenY response

Statistical analysis description:

To demonstrate the non-inferiority of Nimenrix vaccine versus Mencevax ACWY vaccine in term of rSBA vaccine response, the standardized asymptotic 95% CI for the difference in rSBA vaccine response rate for each of the meningococcal serogroups (Nimenrix Group rate minus Mencevax ACWY Group rate) one month after vaccination was computed.

Comparison groups	Nimenrix Group v Mencevax ACWY Group
Number of subjects included in analysis	876
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Parameter estimate	Rate difference
Point estimate	15.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.89
upper limit	21.37

Notes:

[4] - Criterion for non-inferiority: the lower limit of the 2-sided standardized asymptotic 95% confidence interval for the group difference [Nimenrix Group minus Mencevax ACWY Group] in the percentage of subjects with bactericidal vaccine response was greater than or equal to the pre-defined clinical limit of -10%

Statistical analysis title	Difference in % subjects with rSBA-MenA response.2

Statistical analysis description:

To demonstrate the non-inferiority of Nimenrix vaccine versus Mencevax ACWY vaccine in term of rSBA vaccine response, the standardized asymptotic 95% CI for the difference in rSBA vaccine response rate for each of the meningococcal serogroups [Nimenrix Group (without subjects of excluded center) rate minus Mencevax ACWY Group (without subjects of the excluded center) rate] one month after vaccination was computed.

Comparison groups	Nimenrix Group (without subjects of excluded center) v Mencevax ACWY Group (without subjects of the excluded center)

Number of subjects included in analysis	505
Analysis specification	Post-hoc
Analysis type	non-inferiority[5]
Parameter estimate	Rate difference
Point estimate	9.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.17
upper limit	18.54

Notes:

[5] - Criterion for non-inferiority: the lower limit of the 2-sided standardized asymptotic 95% confidence interval for the group difference [Nimenrix
Group (without subjects of exclude center) minus Mencevax ACWY Group (without subjects of the excluded center)] in the percentage of subjects with bactericidal vaccine response was greater than or equal to the pre-defined clinical limit of -10%.

Statistical analysis title	Difference in % subjects with rSBA-MenC response.2

Statistical analysis description:

To demonstrate the non-inferiority of Nimenrix vaccine versus Mencevax ACWY vaccine in term of rSBA vaccine response, the standardized asymptotic 95% CI for the difference in rSBA vaccine response rate for each of the meningococcal serogroups [Nimenrix Group (without
subjects of excluded center) rate minus Mencevax ACWY Group (without subjects of the excluded center) rate] one month after vaccination was computed.

Comparison groups	Nimenrix Group (without subjects of excluded center) v Mencevax ACWY Group (without subjects of the excluded center)
Number of subjects included in analysis	505
Analysis specification	Post-hoc
Analysis type	non-inferiority[6]
Parameter estimate	Rates Difference
Point estimate	-0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.11
upper limit	4.45

Notes:

[6] - Criterion for non-inferiority: the lower limit of the 2-sided standardized asymptotic 95% confidence interval for the group difference [Nimenrix Group (without subjects of excluded center) minus Mencevax ACWY Group (without subjects of the excluded center)] in the percentage of subjects with bactericidal vaccine response was greater than or equal to the pre-defined clinical limit of -10%.

Statistical analysis title	Difference in % subjects withrSBA-MenW135response2

Statistical analysis description:

To demonstrate the non-inferiority of Nimenrix vaccine versus Mencevax ACWY vaccine in term of rSBA vaccine response, the standardized asymptotic 95% CI for the difference in rSBA vaccine response rate for each of the meningococcal serogroups [Nimenrix Group rate (without subjects of excluded center) minus Mencevax ACWY Group (without subjects of the excluded center) rate] one month after vaccination was computed.

Comparison groups	Nimenrix Group (without subjects of excluded center) v Mencevax ACWY Group (without subjects of the excluded center)

Number of subjects included in analysis	505
Analysis specification	Post-hoc
Analysis type	non-inferiority[7]
Parameter estimate	Rate difference
Point estimate	4.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	10.98

Notes:

[7] - Criterion for non-inferiority: the lower limit of the 2-sided standardized asymptotic 95% confidence interval for the group difference [Nimenrix Group (without subjects of excluded center) minus Mencevax ACWY Group (without subjects of the excluded center)] in the percentage of subjects with bactericidal vaccine response was greater than or equal to the pre-defined clinical limit of -10%

Statistical analysis title	Difference in % subjects with rSBA-MenY response.2

Statistical analysis description:

To demonstrate the non-inferiority of Nimenrix vaccine versus Mencevax ACWY vaccine in term of rSBA vaccine response, the standardized asymptotic 95% CI for the difference in rSBA vaccine response rate for each of the meningococcal serogroups [Nimenrix Group (without subjects of excluded center) rate minus Mencevax ACWY Group (without subjects of the excluded center) rate] one month after vaccination was computed.

Comparison groups	Nimenrix Group (without subjects of excluded center) v Mencevax ACWY Group (without subjects of the excluded center)
Number of subjects included in analysis	505
Analysis specification	Post-hoc
Analysis type	non-inferiority[8]
Parameter estimate	Rate difference
Point estimate	16.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.52
upper limit	24.4

Notes:

[8] - Criterion for non-inferiority: the lower limit of the 2-sided standardized asymptotic 95% confidence interval for the group difference [Nimenrix Group (without subjects of excluded center) minus Mencevax ACWY Group (without subjects of the excluded center)] in the percentage of subjects with bactericidal vaccine response was greater than or equal to the pre-defined clinical limit of -10%.

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

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

End point description:

End point type	Primary

End point timeframe:

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

End point values	Nimenrix Group	Mencevax ACWY Group	109067 Nimenrix Group	109067 Mencevax Group
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	768	257	935	312
Units: Subjects				
Subjects with Grade 3 symptoms	12	1	22	7

Statistical analyses

Statistical analysis title	Ratio of % 109067 subjects with Grade 3 symptoms

Statistical analysis description:

To demonstrate the non-inferiority of Nimenrix vaccine versus Mencevax vaccine in term of incidence of any Grade 3 general (solicited and unsolicited) symptom, the 2-sided standardised asymptotic 95% CI for the ratio between Nimenrix and Mencevax (Nimenrix over Mencevax) in the percentage of subjects with any grade 3 general symptom within 4 days after vaccination was computed for the safety analysis in study MenACWY-TT-035.

Comparison groups	109067 Nimenrix Group v 109067 Mencevax Group
Number of subjects included in analysis	1247
Analysis specification	Pre-specified
Analysis type	non-inferiority[9]
P-value	= 0.9116
Method	Standardized asymptotic method
Parameter estimate	Risk ratio (RR)
Point estimate	1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.46
upper limit	2.38

Notes:

[9] - Criterion for non-inferiority: the upper limit of the 2-sided standardized asymptotic 95% CI for the ratio of the percentages of subjects with any Grade 3 general symptom was lower than or equal to the pre-defined clinical limit of 3.0

Statistical analysis title	Ratio of % 109069 subjects with Grade 3 symptoms

Statistical analysis description:

To demonstrate the non-inferiority of Nimenrix vaccine versus Mencevax vaccine in term of incidence of any Grade 3 general (solicited and unsolicited) symptom, the 2-sided standardised asymptotic 95% CI for the ratio between Nimenrix and Mencevax (Nimenrix over Mencevax) in the percentage of subjects with any grade 3 general symptom within 4 days after vaccination was computed for the safety analysis in study MenACWY-TT-036.

Comparison groups	Nimenrix Group v Mencevax ACWY Group
Number of subjects included in analysis	1025
Analysis specification	Pre-specified
Analysis type	non-inferiority[10]
P-value	= 0.1456
Method	Standardized asymptotic method
Parameter estimate	Risk ratio (RR)
Point estimate	4.02

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	24.6

Notes:

[10] - Criterion for non-inferiority: the upper limit of the 2-sided standardized asymptotic 95% CI for the ratio of the percentages of subjects with any Grade 3 general symptom was lower than or equal to the pre-defined clinical limit of 3.0

Statistical analysis title	Ratio of % pooled subjects with Grade 3 symptoms

Statistical analysis description:

To demonstrate the non-inferiority of Nimenrix vaccine versus Mencevax vaccine in term of incidence of any Grade 3 general (solicited and unsolicited) symptom, the 2-sided standardised asymptotic 95% CI for the ratio between Nimenrix and Mencevax (Nimenrix over Mencevax) in the percentage of subjects with any grade 3 general symptom within 4 days after vaccination was computed for the safety analysis in studies MenACWY-TT-035 and MenACWY-TT-036.

Comparison groups	Nimenrix Group v Mencevax ACWY Group v 109067 Nimenrix Group v 109067 Mencevax Group
Number of subjects included in analysis	2272
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.3653 [11]
Method	Standardized asymptotic method
Parameter estimate	Risk ratio (RR)
Point estimate	1.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	3

Notes:

[11] - Criterion for non-inferiority: the upper limit of the 2-sided standardized asymptotic 95% CI for the ratio of the percentages of subjects with any Grade 3 general symptom was lower than or equal to the pre-defined clinical limit of 3.0

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

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

End point description:

End point type	Primary

End point timeframe:

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

End point values	Nimenrix Group (without subjects of excluded center)	Mencevax ACWY Group (without subjects of the excluded center)	109067 Nimenrix Group	109067 Mencevax Group
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	474	159	935	312

Units: Subjects				
Subjects with Grade 3 symptoms	9	1	22	7

Statistical analyses

Statistical analysis title	Ratio of % 109067 subjects with Grade 3 symptoms
Comparison groups	109067 Nimenrix Group v 109067 Mencevax Group
Number of subjects included in analysis	1247
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.9116
Method	Standardized asymptotic method
Parameter estimate	Risk ratio (RR)
Point estimate	1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.46
upper limit	2.38

Statistical analysis title	Ration of % 109069 subjects with Grade 3 symptoms
Comparison groups	Nimenrix Group (without subjects of excluded center) v Mencevax ACWY Group (without subjects of the excluded center)
Number of subjects included in analysis	633
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.2665
Method	Standardized asymptotic method
Parameter estimate	Risk ratio (RR)
Point estimate	3.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	18.41

Statistical analysis title	Ratio of % pooled subjects with Grade 3 symptoms
Comparison groups	Mencevax ACWY Group (without subjects of the excluded center) v 109067 Mencevax Group v Nimenrix Group (without subjects of excluded center) v 109067 Nimenrix Group

Number of subjects included in analysis	1880
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.5085
Method	Standardized asymptotic method
Parameter estimate	Risk ratio (RR)
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	2.76

Secondary: Number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY titer ≥1:8

End point title	Number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY titer ≥1:8

End point description:

End point type	Secondary

End point timeframe:

Prior to (PRE) and one month (M1) after vaccination

End point values	Nimenrix Group	Mencevax ACWY Group	Nimenrix Group (without subjects of excluded center)	Mencevax ACWY Group (without subjects of the excluded center)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	678	224	390	128
Units: Subjects				
rSBA-MenA, PRE (N=557,191,316,108)	463	148	257	83
rSBA-MenA, M1 (N=674,224,388,128)	674	223	388	128
rSBA-MenC, PRE (N=648,211,369,119)	381	121	209	71
rSBA-MenC, M1 (N=673,224,387,128)	673	224	387	128
rSBA- MenW-135, PRE (N=640,216,363,125)	519	176	285	99
rSBA- MenW-135, M1 (N=678,224,390,128)	677	224	389	128
rSBA-MenY, PRE (N=659,219,380,127)	597	186	341	105
rSBA-MenY, M1 (N=677,224,389,128)	677	224	389	128

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

End point type	Secondary

End point timeframe:

Prior to and one month after vaccination

End point values	Nimenrix Group	Mencevax ACWY Group	Nimenrix Group (without subjects of excluded center)	Mencevax ACWY Group (without subjects of the excluded center)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	678	224	390	128
Units: Titers				
geometric mean (confidence interval 95%)				
rSBA-MenA, PRE (N=557,191,316,108)	208.1 (176.4 to 245.5)	155.9 (113.8 to 213.7)	187.7 (149.6 to 235.5)	170.9 (110.8 to 263.6)
rSBA-MenA, M1 (N=674,224,388,128)	5928.5 (5557.4 to 6324.3)	2947.2 (2611.7 to 3325.7)	6688.5 (6162.7 to 7259.2)	3401.4 (2964.6 to 3902.5)
rSBA-MenC, PRE (N=648,211,369,119)	44.1 (37.3 to 52.2)	40.9 (30.2 to 55.3)	43.2 (34.3 to 54.5)	47.9 (31.5 to 73)
rSBA-MenC, M1 (N=673,224,387,128)	13109.8 (11939.1 to 14395.2)	8222 (6807.5 to 9930.4)	11184.2 (9781.6 to 12787.9)	8459.6 (6483.5 to 11038.2)
rSBA- MenW-135, PRE (N=640,216,363,125)	109.4 (94.6 to 126.6)	112.2 (87.2 to 144.3)	96.9 (79.4 to 118.1)	104.9 (74 to 148.7)
rSBA- MenW-135, M1 (N=678,224,390,128)	8246.6 (7638.8 to 8902.7)	2632.7 (2299.3 to 3014.4)	9538.9 (8589.4 to 10593.3)	3303.4 (2790.6 to 3910.4)
rSBA-MenY, PRE (N=659,219,380,127)	348.3 (303.5 to 399.7)	299 (225.2 to 397)	319.9 (265 to 386.3)	286 (193.1 to 423.5)
rSBA-MenY, M1 (N=677,224,389,128)	14086.5 (13168 to 15069)	5066.3 (4463.1 to 5750.9)	16379 (14958.3 to 17934.5)	5772.9 (4856.6 to 6862.1)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-tetanus toxoid (Anti-TT) > 0.1 IU/mL

End point title	Number of subjects with anti-tetanus toxoid (Anti-TT) > 0.1 IU/mL

End point description:

End point type	Secondary

End point timeframe:
Prior to and one month after vaccination

End point values	Nimenrix Group	Mencevax ACWY Group	Nimenrix Group (without subjects of excluded center)	Mencevax ACWY Group (without subjects of the excluded center)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	679	224	391	128
Units: Subjects				
Anti-TT, PRE (N=679,224,391,128)	439	155	357	120
Anti-TT, M1 (N=679,224,391,128)	662	157	389	119

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-TT antibody concentrations

End point title	Anti-TT antibody concentrations

End point description:

End point type	Secondary

End point timeframe:
Prior to and one month after vaccination

End point values	Nimenrix Group	Mencevax ACWY Group	Nimenrix Group (without subjects of excluded center)	Mencevax ACWY Group (without subjects of the excluded center)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	679	224	391	128
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-TT, PRE (N=679,224,391,128)	0.367 (0.321 to 0.419)	0.41 (0.326 to 0.516)	1.035 (0.9 to 1.191)	1.153 (0.907 to 1.464)
Anti-TT, M1 (N=679,224,391,128)	10.305 (9.131 to 11.631)	0.459 (0.364 to 0.58)	18.089 (16.314 to 20.058)	1.212 (0.948 to 1.549)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-PSA, anti-PSC, anti-PSW-135, and anti-PSY concentrations ≥ 0.3 µg/mL and ≥ 2.0 µg/mL

End point title	Number of subjects with anti-PSA, anti-PSC, anti-PSW-135, and anti-PSY concentrations ≥ 0.3 µg/mL and ≥ 2.0 µg/mL

End point description:

End point type	Secondary

End point timeframe:

Prior to and one month after vaccination

End point values	Nimenrix Group	Mencevax ACWY Group	Nimenrix Group (without subjects of excluded center)	Mencevax ACWY Group (without subjects of the excluded center)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	347	114	204	68
Units: Subjects				
Anti-PSA ≥ 0.3 ug/mL, PRE (N=322,102,189,59)	235	75	130	40
Anti-PSA ≥ 0.3 ug/mL, M1 (N=341,107,194,59)	341	107	194	59
Anti-PSC ≥ 0.3 ug/mL, PRE (N=335,108,190,60)	50	21	25	13
Anti-PSC ≥ 0.3 ug/mL, M1 (N=331,107,188,60)	331	107	188	60
Anti-PSW-135 ≥ 0.3 ug/mL, PRE (N=340,111,204,64)	40	8	23	6
Anti-PSW-135 ≥ 0.3 ug/mL, M1 (N=344,114,205,66)	340	113	203	66
Anti-PSY ≥ 0.3 ug/mL, PRE (N=347,114,206,68)	49	16	28	11
Anti-PSY ≥ 0.3 ug/mL, M1 (N=342,114,201,66)	342	113	201	66
Anti-PSA ≥ 2 ug/mL, PRE (N=322,102,189,59)	130	40	78	24
Anti-PSA ≥ 2 ug/mL, M1 (N=341,107,194,59)	341	107	194	59
Anti-PSC ≥ 2 ug/mL, PRE (N=335,108,190,60)	17	10	8	6
Anti-PSC ≥ 2 ug/mL, M1 (N=331,107,188,60)	324	106	181	59
Anti-PSW-135 ≥ 2 ug/mL, PRE (N=340,111,204,64)	9	3	5	2
Anti-PSW-135 ≥ 2 ug/mL, M1 (N=344,114,205,66)	327	106	192	61
Anti-PSY ≥ 2 ug/mL, PRE (N=347,114,206,68)	12	8	5	7
Anti-PSY ≥ 2 ug/mL, M1 (N=342,114,201,66)	336	111	195	65

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PSA, anti-PSC, anti-PSW-135, and anti-PSY antibody concentrations

End point title	Anti-PSA, anti-PSC, anti-PSW-135, and anti-PSY antibody concentrations

End point description:

End point type	Secondary

End point timeframe:

Prior to and one month after vaccination

End point values	Nimenrix Group	Mencevax ACWY Group	Nimenrix Group (without subjects of excluded center)	Mencevax ACWY Group (without subjects of the excluded center)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	347	114	206	68
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PSA, PRE (N=322,102,189,59)	1.05 (0.88 to 1.24)	1.04 (0.77 to 1.39)	1 (0.79 to 1.28)	1.04 (0.68 to 1.6)
Anti-PSA, M1 (N=341,107,194,59)	86.06 (75.35 to 98.29)	44.06 (34.4 to 56.42)	85.68 (71.24 to 103.04)	51.87 (36.86 to 72.98)
Anti-PSC, PRE (N=335,108,190,60)	0.21 (0.19 to 0.24)	0.25 (0.2 to 0.3)	0.2 (0.18 to 0.23)	0.26 (0.19 to 0.35)
Anti-PSC, M1 (N=331,107,188,60)	22.83 (20.42 to 25.52)	43.24 (35.8 to 52.23)	17.71 (15.13 to 20.72)	40.09 (30.73 to 52.31)
Anti-PSW-135, PRE (N=340,111,204,64)	0.18 (0.17 to 0.2)	0.18 (0.16 to 0.21)	0.18 (0.17 to 0.2)	0.19 (0.15 to 0.24)
Anti-PSW-135, M1 (N=344,114,205,66)	17.82 (15.34 to 20.7)	13.22 (10.47 to 16.68)	15.48 (12.73 to 18.82)	14.5 (10.72 to 19.62)
Anti-PSY, PRE (N=347,114,206,68)	0.2 (0.18 to 0.22)	0.22 (0.18 to 0.28)	0.19 (0.17 to 0.22)	0.25 (0.18 to 0.35)
Anti-PSY, M1 (N=342,114,201,66)	23.77 (20.95 to 26.98)	17.97 (14.3 to 22.59)	20.95 (17.61 to 24.94)	18.79 (13.94 to 25.32)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any solicited local symptoms

End point title	Number of subjects with any solicited local symptoms

End point description:

End point type	Secondary

End point timeframe:

During the 4-day (Day 0 to Day 3) period after vaccination

End point values	Nimenrix Group	Mencevax ACWY Group	Nimenrix Group (without subjects of excluded center)	Mencevax ACWY Group (without subjects of the excluded center)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	763	254	469	156
Units: Subjects				
Any Pain	200	68	174	49
Any Redness	94	16	75	11
Any Swelling	71	16	61	14

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any solicited general symptoms

End point title	Number of subjects with any solicited general symptoms

End point description:

End point type	Secondary

End point timeframe:

During the 4-day (Day 0 to Day 3) period after vaccination

End point values	Nimenrix Group	Mencevax ACWY Group	Nimenrix Group (without subjects of excluded center)	Mencevax ACWY Group (without subjects of the excluded center)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	763	254	469	156
Units: Subjects				
Any Fatigue	109	36	75	22
Any Fever (Axillary)	55	13	39	10
Any Gastrointestinal symptoms	35	11	26	8
Any Headache	102	27	58	12

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any unsolicited adverse events

End point title	Number of subjects with any unsolicited adverse events

End point description:

End point type	Secondary

End point timeframe:

Up to one month after vaccination

End point values	Nimenrix Group	Mencevax ACWY Group	Nimenrix Group (without subjects of excluded center)	Mencevax ACWY Group (without subjects of the excluded center)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	768	257	474	159
Units: Subjects				
Any AEs	72	26	38	13

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects with any serious adverse events (SAEs)

End point description:

End point type	Secondary

End point timeframe:

Up to 6 months after vaccination

End point values	Nimenrix Group	Mencevax ACWY Group	Nimenrix Group (without subjects of excluded center)	Mencevax ACWY Group (without subjects of the excluded center)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	768	257	474	159
Units: Subjects				
Any SAEs	3	2	2	2

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with specific adverse events

End point title	Number of subjects with specific adverse events

End point description:

These events included the specific categories of adverse events (AEs) which included rash (e.g. hives, idiopathic thrombocytopenia purpura, petechiae), new onset of chronic illness(es) (NOCIs) (e.g. autoimmune disorders, asthma, type I diabetes and allergies), conditions prompting emergency room (ER) visits 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), any events related to lack of meningococcal vaccine efficacy (i.e. meningococcal disease)*.

End point type	Secondary

End point timeframe:

Up to 6 months after vaccination

End point values	Nimenrix Group	Mencevax ACWY Group	Nimenrix Group (without subjects of excluded center)	Mencevax ACWY Group (without subjects of the excluded center)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	768	257	474	159
Units: Subjects				
Any Rash	6	1	5	1
Any NOCIs	0	0	0	0
Any ER visits	1	0	1	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY titer ≥1:128

End point title	Number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY titer ≥1:128

End point description:

End point type	Secondary

End point timeframe:

Prior to (PRE) and one month (M1) after vaccination

End point values	Nimenrix Group	Mencevax ACWY Group	Nimenrix Group (without subjects of excluded center)	Mencevax ACWY Group (without subjects of the excluded center)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	678	224	390	128
Units: Subjects				
rSBA-MenA, PRE (N=557,191,316,108)	427	128	233	74
rSBA-MenA, M1 (N=674,224,388,128)	674	223	388	128
rSBA-MenC, PRE (N=648,211,369,119)	277	79	153	45
rSBA-MenC, M1 (N=673,224,387,128)	672	223	386	128
rSBAMenW-135, PRE (N=640,216,363,125)	373	120	199	67
rSBAMenW-135, M1 (N=678,224,390,128)	677	223	389	128
rSBA-MenY, PRE (N=659,219,380,127)	538	167	301	96
rSBA-MenY, M1 (N=677,224,389,128)	677	224	389	128

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited local and general adverse events (AEs): during the 4-day (Day 0 to Day 3) period after vaccination
Unsolicited AEs: up to one month after vaccination
Serious AEs and specific AEs: up to 6 month after vaccination (study end)

Adverse event reporting additional description:

The occurrence of reported AEs (all/related) was not available and is encoded as equal to the number of subjects affected.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.0

Reporting groups

Reporting group title	MenACWY-TT

Reporting group description:

Subjects received 1 dose of meningococcal vaccine GSK134612

Reporting group title	MenACWY (without the subjects of the excluded center)

Reporting group description:

Subjects from the MenACWY group who had not GCP issues

Reporting group title	MenACWY-TT (without subjects of the excluded center)

Reporting group description:

Subjects from the MenACWY-TT group who had not GCP issues

Reporting group title	MenACWY

Reporting group description:

Subject received 1 dose of Mencevax™ ACWY

Serious adverse events	MenACWY-TT	MenACWY (without the subjects of the excluded center)	MenACWY-TT (without subjects of the excluded center)
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 768 (0.39%)	2 / 159 (1.26%)	2 / 474 (0.42%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	0 / 768 (0.00%)	1 / 159 (0.63%)	0 / 474 (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
Gastrointestinal disorders			
Peptic ulcer			

subjects affected / exposed	2 / 768 (0.26%)	0 / 159 (0.00%)	2 / 474 (0.42%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Amoebic dysentery			
subjects affected / exposed	1 / 768 (0.13%)	0 / 159 (0.00%)	0 / 474 (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
Appendicitis			
subjects affected / exposed	0 / 768 (0.00%)	1 / 159 (0.63%)	0 / 474 (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
Peritoneal abscess			
subjects affected / exposed	0 / 768 (0.00%)	1 / 159 (0.63%)	0 / 474 (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
Urinary tract infection			
subjects affected / exposed	1 / 768 (0.13%)	0 / 159 (0.00%)	0 / 474 (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

Serious adverse events	MenACWY		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 257 (0.78%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	1 / 257 (0.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Peptic ulcer			

subjects affected / exposed	0 / 257 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Amoebic dysentery			
subjects affected / exposed	0 / 257 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Appendicitis			
subjects affected / exposed	1 / 257 (0.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peritoneal abscess			
subjects affected / exposed	1 / 257 (0.39%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	0 / 257 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	MenACWY-TT	MenACWY (without the subjects of the excluded center)	MenACWY-TT (without subjects of the excluded center)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	200 / 768 (26.04%)	49 / 159 (30.82%)	174 / 474 (36.71%)
General disorders and administration site conditions			
Pain			
alternative assessment type: Systematic			
subjects affected / exposed	200 / 768 (26.04%)	49 / 159 (30.82%)	174 / 474 (36.71%)
occurrences (all)	200	49	174
Redness			
alternative assessment type: Systematic			

subjects affected / exposed	94 / 768 (12.24%)	11 / 159 (6.92%)	75 / 474 (15.82%)
occurrences (all)	94	11	75
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed	71 / 768 (9.24%)	14 / 159 (8.81%)	61 / 474 (12.87%)
occurrences (all)	71	14	61
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	109 / 768 (14.19%)	22 / 159 (13.84%)	75 / 474 (15.82%)
occurrences (all)	109	22	75
Fever			
alternative assessment type: Systematic			
subjects affected / exposed	55 / 768 (7.16%)	10 / 159 (6.29%)	39 / 474 (8.23%)
occurrences (all)	55	10	39
Gastrointestinal			
alternative assessment type: Systematic			
subjects affected / exposed	35 / 768 (4.56%)	8 / 159 (5.03%)	26 / 474 (5.49%)
occurrences (all)	35	8	26
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	102 / 768 (13.28%)	12 / 159 (7.55%)	58 / 474 (12.24%)
occurrences (all)	102	12	58
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	0 / 768 (0.00%)	8 / 159 (5.03%)	13 / 474 (2.74%)
occurrences (all)	0	8	13

Non-serious adverse events	MenACWY		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	68 / 257 (26.46%)		
General disorders and administration site conditions			
Pain			
alternative assessment type: Systematic			
subjects affected / exposed	68 / 257 (26.46%)		
occurrences (all)	68		

Redness			
alternative assessment type: Systematic			
subjects affected / exposed	16 / 257 (6.23%)		
occurrences (all)	16		
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed	16 / 257 (6.23%)		
occurrences (all)	16		
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	36 / 257 (14.01%)		
occurrences (all)	36		
Fever			
alternative assessment type: Systematic			
subjects affected / exposed	13 / 257 (5.06%)		
occurrences (all)	13		
Gastrointestinal			
alternative assessment type: Systematic			
subjects affected / exposed	11 / 257 (4.28%)		
occurrences (all)	11		
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	27 / 257 (10.51%)		
occurrences (all)	27		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	0 / 257 (0.00%)		
occurrences (all)	0		

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