Clinical trial results:
A phase III, open, randomized, controlled, primary vaccination study to demonstrate non-inferiority of GlaxoSmithKline (GSK) Biologicals' meningococcal serogroup ACWY conjugate vaccine compared to licensed MenC-CRM197 conjugate vaccine when administered to healthy subjects aged 2 through 10 years.

Summary

EudraCT number	2007-007837-38
Trial protocol	DE FR
Global end of trial date	08 January 2009

Results information

Result version number	v3 (current)
This version publication date	08 October 2021
First version publication date	04 April 2015
Version creation reason	• Correction of full data set Correction of full data set and alignment between registries.

Trial information

Trial identification

Sponsor protocol code	111414

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00674583
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals , 044 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals , 044 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-PIP01-01
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	14 May 2009
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 September 2008
Global end of trial reached?	Yes
Global end of trial date	08 January 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

One month after vaccination:
•To demonstrate non-inferiority of the MenACWY-TT conjugate vaccine compared to the licensed conjugate vaccine (MenC-CRM197) in terms of serum bactericidal antibody vaccine response to N. meningitidis serogroup C (MenC).

Criterion for assessment of non-inferiority for serogroup C:
The lower limit of the two-sided standardized asymptotic 95% confidence interval (CI) for the group difference (MenACWY-TT Group minus MenC-CRM Group) in the percentages of subjects with vaccine response to meningococcal polysaccharide C serum based on a bactericidal assay using baby rabbit complement (rSBA-MenC) is greater than or equal to the pre-defined clinical limit of –10%.
The vaccine response to MenC is defined as post-vaccination rSBA-MenC titer ≥ 1:32 for initially seronegative subjects (i.e. rSBA-MenC titer < 1:8) and at least a 4-fold increase in rSBA-MenC titers from pre to post-vaccination for initially seropositive (i.e. rSBA-MenC titer ≥ 1:8) subjects.

Protection of trial subjects:

Written informed consent was obtained from each subject’s parent/guardian prior to the performance of any study-specific procedures. The investigator was required to notify GSK Biologicals’ Study Contact for Serious Adverse Event by fax, within 24 hours of his/her becoming aware of the SAE. After the initial AE/SAE report, the investigator was required to proactively follow each subject and provide further information to GSK Biologicals on the subject’s condition.
All AEs and SAEs documented at a previous visit/contact and designated as not recovered/not resolved or recovering/resolving were reviewed at subsequent visits/contacts.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 May 2008
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	France: 155
Country: Number of subjects enrolled	Germany: 259
Worldwide total number of subjects	414
EEA total number of subjects	414

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)	414
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.

Period 1

Period 1 title	Overall trial (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:

Healthy male or female subjects between, and including 2 and 10 years of age, intramuscularly received 1 dose of Nimenrix vaccine into the non-dominant deltoid region, at Day 0.

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

Dosage and administration details:

1 dose by intramuscular administration in the non-dominant deltoid/thigh region at Day 0.

Arm title	Menjugate Group

Arm description:

Healthy male or female subjects between, and including 2 and 10 years of age, intramuscularly received 1 dose of Menjugate vaccine into the non-dominant thigh region, at Day 0.

Arm type	Active comparator
Investigational medicinal product name	Menjugate
Investigational medicinal product code	
Other name	MenC-CRM197
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose by intramuscular administration in the non-dominant deltoid/thigh region at Day 0.

Number of subjects in period 1	Nimenrix Group	Menjugate Group
Started	311	103
Completed	311	103

Baseline characteristics

Reporting groups	
Reporting group title	Nimenrix Group
Reporting group description:	
Healthy male or female subjects between, and including 2 and 10 years of age, intramuscularly received 1 dose of Nimenrix vaccine into the non-dominant deltoid region, at Day 0.	
Reporting group title	Menjugate Group
Reporting group description:	
Healthy male or female subjects between, and including 2 and 10 years of age, intramuscularly received 1 dose of Menjugate vaccine into the non-dominant thigh region, at Day 0.	

Reporting group values	Nimenrix Group	Menjugate Group	Total
Number of subjects	311	103	414
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	311	103	414
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	5.6	5.6	
standard deviation	± 2.52	± 2.32	-
Gender categorical Units: Subjects			
Female	163	51	214
Male	148	52	200

End points

End points reporting groups

Reporting group title	Nimenrix Group
Reporting group description:	
Healthy male or female subjects between, and including 2 and 10 years of age, intramuscularly received 1 dose of Nimenrix vaccine into the non-dominant deltoid region, at Day 0.	
Reporting group title	Menjugate Group
Reporting group description:	
Healthy male or female subjects between, and including 2 and 10 years of age, intramuscularly received 1 dose of Menjugate vaccine into the non-dominant thigh region, at Day 0.	

Primary: Number of subjects with vaccine response to meningococcal serogroup C serum based on a bactericidal assay using baby rabbit complement (rSBA-MenC) antibody

End point title	Number of subjects with vaccine response to meningococcal serogroup C serum based on a bactericidal assay using baby rabbit complement (rSBA-MenC) antibody
End point description:	
Vaccine response to MenC was defined as: -for initially seronegative subjects [i.e. rSBA-MenC titer below (<) 1:8], antibody titer greater than or equal to (≥) 1:32; -for initially seropositive (i.e. rSBA-MenC titer ≥ 1:8), antibody titer post-vaccination ≥ 4-fold the pre-vaccination antibody titer.	
End point type	Primary
End point timeframe:	
One month after the vaccination (Month 1)	

End point values	Nimenrix Group	Menjugate Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	268	92		
Units: Subjects				
rSBA-MenC	254	88		

Statistical analyses

Statistical analysis title	Difference in % of subjects with vaccine response
Statistical analysis description:	
To demonstrate the non-inferiority of the Nimenrix group compared to the Menjugate group, two-sided standardized asymptotic 95% confidence interval (CI) for the groups difference [Nimenrix group minus Menjugate group] in the percentages of subjects with bactericidal vaccine response to MenC was computed.	
Comparison groups	Nimenrix Group v Menjugate Group

Number of subjects included in analysis	360
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Difference in percentage
Point estimate	-0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.25
upper limit	5.75

Notes:

[1] - For MenC serogroup, the two-sided standardized asymptotic 95% CI for the group difference (Nimenrix Group minus Menjugate Group) in the percentages of subjects with bactericidal vaccine response was computed.

Secondary: Meningococcal serogroup A (rSBA) antibody titers by serogroup

End point title	Meningococcal serogroup A (rSBA) antibody titers by serogroup

End point description:

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

End point type	Secondary

End point timeframe:

Prior to (Month 0) and one month after vaccination (Month 1)

End point values	Nimenrix Group	Menjugate Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	296	97		
Units: Titers				
geometric mean (confidence interval 95%)				
rSBA-MenA, Month 0 [N=227;76]	31.5 (23.3 to 42.5)	25.9 (15.6 to 43)		
rSBA-MenA, Month 1 [N=294;82]	6236.1 (5574.5 to 6976.3)	27.2 (15.6 to 47.4)		
rSBA-MenC, Month 0 [N=270;94]	22.7 (18.1 to 28.4)	19.4 (13.1 to 28.8)		
rSBA-MenC, Month 1 [N=293;97]	2794.8 (2393.5 to 3263.3)	5291.6 (3814.6 to 7340.5)		
rSBA-MenW-135, Month 0 [N=282;92]	83.2 (67.9 to 102)	70.2 (48.5 to 101.6)		
rSBA-MenW-135, Month 1 [N=296;95]	8549.5 (7618.5 to 9594.3)	87.3 (58.5 to 130.4)		
rSBA-MenY, Month 0 [N=285;90]	153.6 (125.3 to 188.3)	107.4 (71.4 to 161.6)		
rSBA-MenY, Month 1 [N=295;95]	8360.7 (7447.3 to 9386.1)	128.2 (83.8 to 196.2)		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Anti-PSA, anti-PSC, anti-PSW-135 and anti-PSY antibody concentrations were expressed as geometric mean concentrations (GMCs) and tabulated as micrograms per milliliter (µg/mL).

End point type	Secondary

End point timeframe:

Prior to (Month 0) and one month after vaccination (Month 1)

End point values	Nimenrix Group	Menjugate Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	149	52		
Units: concentration				
geometric mean (confidence interval 95%)				
Anti-PSA, Month 0 [N=148;52]	0.2 (0.17 to 0.22)	0.22 (0.17 to 0.29)		
Anti-PSA, Month 1 [N=149;50]	32.45 (26.57 to 39.63)	0.31 (0.19 to 0.49)		
Anti-PSc, Month 0 [N=147;52]	0.18 (0.16 to 0.2)	0.2 (0.16 to 0.25)		
Anti-PSC, Month 1 [N=149;52]	14.95 (12.89 to 17.34)	18.07 (13.88 to 23.51)		
Anti-PSW-135, Month 0 [N=144;47]	0.17 (0.15 to 0.18)	0.17 (0.14 to 0.2)		
Anti-PSW-135, Month 1 [N=144;47]	6.96 (5.72 to 8.47)	0.18 (0.15 to 0.22)		
Anti-PSY, Month 0 [N=147;47]	0.16 (0.15 to 0.17)	0.16 (0.15 to 0.17)		
Anti-PSY, Month 1 [N=144;47]	14.15 (11.66 to 17.17)	0.17 (0.15 to 0.19)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects between 2 and 5 years of age with any and Grade 3 solicited local symptoms

End point title	Number of subjects between 2 and 5 years of age with any and Grade 3 solicited local symptoms

End point description:

Solicited symptoms assessed were: pain, redness and swelling. Any = occurrence of any local symptom regardless of their intensity grade. Grade 3 Pain = cried when limb was moved/spontaneously painful. Grade 3 Redness and Swelling= redness/swelling spreading beyond (>) 30 millimeters (mm).

End point type	Secondary

End point timeframe:

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

End point values	Nimenrix Group	Menjugate Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	162	53		
Units: Subjects				
Any Pain	45	15		
Grade 3 Pain	0	1		
Any Redness	57	21		
Grade 3 Redness	11	8		
Any Swelling	43	13		
Grade 3 Swelling	7	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects between 6 and 10 years of age with any and Grade 3 solicited local symptoms

End point title	Number of subjects between 6 and 10 years of age with any and Grade 3 solicited local symptoms

End point description:

Solicited symptoms assessed were: pain, redness and swelling. Any = occurrence of any local symptom regardless of their intensity grade. Grade 3 Pain = pain that prevented normal activity. Grade 3 Redness and Swelling= redness/swelling spreading beyond (>) 50 millimeters (mm).

End point type	Secondary

End point timeframe:

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

End point values	Nimenrix Group	Menjugate Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	50		
Units: Subjects				
Any Pain	65	27		
Grade 3 Pain	3	3		
Any Redness	58	19		
Grade 3 Redness	9	5		
Any Swelling	44	15		
Grade 3 Swelling	4	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects between 2 and 5 years of age with any, Grade 3 and related solicited general symptoms

End point title	Number of subjects between 2 and 5 years of age with any, Grade 3 and related solicited general symptoms

End point description:

Solicited general symptoms assessed were drowsiness, fever[defined as oral temperature ≥ 37.5 degrees Celsius (°C)], irritability and loss of appetite. Any = occurrence of the general symptom regardless of intensity grade and relationship to vaccination. Grade 3 Symptom = symptom that prevented normal activity. Grade 3 Loss of appetite = did not eat at all. Grade 3 Fever = fever > 39.5°C. Related = general symptoms assessed by the investigator as causally related to vaccination.

End point type	Secondary

End point timeframe:

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

End point values	Nimenrix Group	Menjugate Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	162	53		
Units: Subjects				
Any Drowsiness	23	6		
Grade 3 Drowsiness	0	1		
Related Drowsiness	15	6		
Any Fever	9	3		
Grade 3 Fever	0	0		
Related Fever	9	3		
Any Irritability	25	6		
Grade 3 Irritability	1	1		
Related Irritability	16	5		
Any Loss of appetite	17	5		
Grade 3 Loss of appetite	0	0		
Related Loss of appetite	9	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects between 6 and 10 years of age with any, Grade 3 and related solicited general symptoms

End point title	Number of subjects between 6 and 10 years of age with any, Grade 3 and related solicited general symptoms

End point description:

Solicited general symptoms assessed were fatigue, fever(defined as oral temperature ≥ 37.5 °C), gastrointestinal and headache. Any = occurrence of the general symptom regardless of intensity grade and relationship to vaccination. Grade 3 Symptom = symptom that prevented normal activity. Grade 3 Loss of appetite = did not eat at all. Grade 3 Fever = fever > 39.5°C. Related = general symptoms assessed by the investigator as causally related to vaccination.

End point type	Secondary

End point timeframe:

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

End point values	Nimenrix Group	Menjugate Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	148	50		
Units: Subjects				
Any Fatigue	33	11		
Grade 3 Fatigue	4	0		
Related Fatigue	29	7		
Any Fever (Orally)	10	1		
Grade 3 Fever (Orally)	0	0		
Related Fever (Orally)	9	0		
Any Gastrointestinal	22	4		
Grade 3 Gastrointestinal	1	0		
Related Gastrointestinal	13	3		
Any Headache	30	4		
Grade 3 Headache	2	0		
Related Headache	24	2		

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 included: - rash (hives, idiopathic thrombocytopenic purpura, petechiae); - new onset of chronic illness(es) (NOCI) (e.g. autoimmune disorders, asthma, type I diabetes and allergies); - conditions prompting emergency room (ER) visits.

End point type	Secondary

End point timeframe:

Up to 6 months after vaccination (Month 6)

End point values	Nimenrix Group	Menjugate Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	311	103		
Units: Subjects				
Any Rash(es)	8	1		
Any NOCI(s)	1	1		
Any ER visit(s)	11	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited adverse events(AEs)

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

End point description:

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

End point type	Secondary

End point timeframe:

Up to one month (Day 0-Day 30) post-vaccination period

End point values	Nimenrix Group	Menjugate Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	311	103		
Units: Subjects				
Unsolicited symptom (s)	55	20		

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:

Up to six months after vaccination (Month 6)

End point values	Nimenrix Group	Menjugate Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	311	103		
Units: Subjects				
SAE (s)	6	1		

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. Unsolicited adverse events: Up to one month (Day 0-Day 30) after vaccination.

Adverse event reporting additional description:

The solicited local and general symptoms were only collected from those subjects who filled in their symptom sheets.
The number of occurrences reported for solicited symptoms, AEs, and SAEs was not available for posting. The number of subjects affected by each specific event was indicated as the number of occurrences.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	11.1

Reporting groups

Reporting group title	Menjugate Group

Reporting group description:

Subjects received 1 dose of Menjugate vaccine administered intramuscularly in the non-dominant deltoid/thigh region at Day 0.

Reporting group title	Nimenrix Group

Reporting group description:

Subjects received 1 dose of Nimenrix vaccine administered intramuscularly in the non-dominant deltoid/thigh region at Day 0.

Serious adverse events	Menjugate Group	Nimenrix Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 103 (0.97%)	6 / 311 (1.93%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Abdominal injury			
subjects affected / exposed	0 / 103 (0.00%)	1 / 311 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Accidental poisoning			
subjects affected / exposed	0 / 103 (0.00%)	1 / 311 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			

subjects affected / exposed	0 / 103 (0.00%)	1 / 311 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Convulsion			
subjects affected / exposed	0 / 103 (0.00%)	1 / 311 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 103 (0.00%)	1 / 311 (0.32%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 103 (0.00%)	1 / 311 (0.32%)	
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 / 103 (0.97%)	0 / 311 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasopharyngitis			
subjects affected / exposed	0 / 103 (0.00%)	1 / 311 (0.32%)	
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	Menjugate Group	Nimenrix Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	63 / 103 (61.17%)	181 / 311 (58.20%)	
General disorders and administration site conditions			

Pain			
alternative assessment type: Systematic			
subjects affected / exposed[1]	42 / 103 (40.78%)	110 / 310 (35.48%)	
occurrences (all)	42	110	
Redness			
alternative assessment type: Systematic			
subjects affected / exposed[2]	40 / 103 (38.83%)	115 / 310 (37.10%)	
occurrences (all)	40	115	
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed[3]	28 / 103 (27.18%)	87 / 310 (28.06%)	
occurrences (all)	28	87	
Drowsiness (< 6 years)	Additional description: This solicited general symptom was assessed only for subjects between 2 to 5 years of age, from the two groups.		
alternative assessment type: Systematic			
subjects affected / exposed[4]	6 / 53 (11.32%)	23 / 162 (14.20%)	
occurrences (all)	6	23	
Fever			
alternative assessment type: Systematic			
subjects affected / exposed[5]	4 / 103 (3.88%)	19 / 310 (6.13%)	
occurrences (all)	4	19	
Irritability (< 6 years)	Additional description: This solicited general symptom was assessed only for subjects between 2 to 5 years of age, from the two groups.		
alternative assessment type: Systematic			
subjects affected / exposed[6]	6 / 53 (11.32%)	25 / 162 (15.43%)	
occurrences (all)	6	25	
Loss of appetite (< 6 years)	Additional description: This solicited general symptom was assessed only for subjects between 2 to 5 years of age, from the two groups.		
alternative assessment type: Systematic			
subjects affected / exposed[7]	5 / 53 (9.43%)	17 / 162 (10.49%)	
occurrences (all)	5	17	
Fatigue (≥ 6 years)	Additional description: This solicited general symptom was assessed only for subjects between 6 to 10 years of age, from the two groups.		
alternative assessment type: Systematic			
subjects affected / exposed[8]	11 / 50 (22.00%)	33 / 148 (22.30%)	
occurrences (all)	11	33	
Gastrointestinal (≥ 6 years)	Additional description: This solicited general symptom was assessed only for subjects between 6 to 10 years of age, from the two groups.		

alternative assessment type: Systematic			
subjects affected / exposed[9]	4 / 50 (8.00%)	22 / 148 (14.86%)	
occurrences (all)	4	22	
Headache (≥ 6 years)	Additional description: This solicited general symptom was assessed only for subjects between 6 to 10 years of age, from the two groups.		
alternative assessment type: Systematic			
subjects affected / exposed[10]	4 / 50 (8.00%)	30 / 148 (20.27%)	
occurrences (all)	4	30	

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 solicited local and general symptoms were only collected from those subjects who filled in their symptom sheets.

[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 solicited local and general symptoms were only collected from those subjects who filled in their symptom sheets.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The solicited local and general symptoms were only collected from those subjects who filled in their symptom sheets.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The solicited local and general symptoms were only collected from those subjects who filled in their symptom sheets. This solicited general symptom was assessed only for subjects between 2 to 5 years of age, from the two groups.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The solicited local and general symptoms were only collected from those subjects who filled in their symptom sheets.

[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 solicited local and general symptoms were only collected from those subjects who filled in their symptom sheets. This solicited general symptom was assessed only for subjects between 2 to 5 years of age, from the two groups.

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The solicited local and general symptoms were only collected from those subjects who filled in their symptom sheets. This solicited general symptom was assessed only for subjects between 2 to 5 years of age, from the two groups.

[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 solicited local and general symptoms were only collected from those subjects who filled in their symptom sheets. This solicited general symptom was assessed only for subjects between 6 to 10 years of age, from the two groups.

[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 solicited local and general symptoms were only collected from those subjects who filled in their symptom sheets. This solicited general symptom was assessed only for subjects between 6 to 10 years of age, from the two groups.

[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.
Justification: The solicited local and general symptoms were only collected from those subjects who filled in their symptom sheets. This solicited general symptom was assessed only for subjects between 6 to 10 years of age, from the two groups.

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