Clinical trial results:
A Phase 2, Randomized, Comparative, Multicenter Observer-Blind Study Evaluating the Safety and Immunogenicity of the New Liquid Formulation of Novartis Meningococcal C Conjugate Vaccine and of the Novartis Lyophilized Meningococcal C Conjugate Vaccine Manufactured at Two Different Sites, in Healthy Toddlers

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

Summary

EudraCT number	2011-000395-34
Trial protocol	PL
Global end of trial date	02 November 2012

Results information

Result version number	v2 (current)
This version publication date	04 June 2016
First version publication date	01 January 2015
Version creation reason	• Correction of full data set re-QC study needed because of EudraCT system glitch and updates to results are required.

Trial information

Trial identification

Sponsor protocol code	V14_57

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01434680
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Vaccines
Sponsor organisation address	Via Fiorentina, 1 , Siena, Italy, 53100
Public contact	Posting Director, Novartis Vaccines, RegistryContactVaccinesUS@novartis.com
Scientific contact	Posting Director, Novartis Vaccines, RegistryContactVaccinesUS@novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 May 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 November 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The equivalence of MenC-CRM liquid to MenC-CRM EMV and the equivalence of MenC-CRM ROS to MenC-CRM EMV were to be simultaneously assessed with adjustment for multiple comparisons.

1. To demonstrate the equivalence of MenC-CRM liquid to MenC-CRM EMV when administered to toddlers, as measured by human serum bactericidal activity (hSBA) geometric mean titers (GMTs) against N meningitidis serogroup C, approximately 28 days after a single vaccination.

2. To demonstrate the equivalence of MenC-CRM ROS to MenC-CRM EMV when administered to toddlers, as measured by human serum bactericidal activity (hSBA) geometric mean titers (GMTs) against N meningitidis serogroup C, approximately 28 days after a single vaccination.

Protection of trial subjects:

This clinical study was designed and implemented and reported in accordance with the International Conference on Harmonization (ICH) Harmonized Tripartite Guidelines for Good Clinical Practice (GCP), with applicable local regulations (including European Directive 2001/20/EC, US Code of Federal Regulations Title 21, and Japanese Ministry of Health, Labor, and Welfare), and with the ethical principles laid down in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 September 2011
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	Poland: 992
Worldwide total number of subjects	992
EEA total number of subjects	992

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	991
Children (2-11 years)	1
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:

Subjects were recruited from 11 centers.

Pre-assignment

Screening details:

Toddlers of both genders (aged 12 through 23 months of age) generally in good health were eligible for this study. For toddlers to be enrolled, the parent(s) or legally acceptable representative(s) had to provide written informed consent and had to be available for all study visits. Serious, acute, or chronic illnesses were reasons for exclusion.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

The study was designed as an observer-blind study. An unblinded administrator administered the study vaccine randomly assigned for the individual subject. The subjects' parents, investigator and study site personnel involved in the conduct of the trial and safety follow-up were blinded to which study vaccine each subject received. NVD personnel were blinded in EDC, except the users with an 'unblinded role' in EDC.

Arms

Are arms mutually exclusive?	Yes
Arm title	MenC-CRM LIQ

Arm description:

Subjects received 1 injection of MenC-CRM vaccine, liquid formulation

Arm type	Experimental
Investigational medicinal product name	Meningococcal C-CRM conjugated
Investigational medicinal product code	MenC-CRM liquid
Other name	
Pharmaceutical forms	Powder and solvent for suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

1 single dose 0.5 mL per injection

Arm title	MenC-CRM ROS

Arm description:

Subjects received 1 injection of MenC-CRM vaccine, lyophilized formulation produced with drug substance manufactured at Rosia, Italy

Arm type	Active comparator
Investigational medicinal product name	Meningococcal C-CRM conjugated
Investigational medicinal product code	MenC-CRM ROS
Other name	
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 single dose 0.5 mL per injection

Arm title	MenC-CRM EMV

Arm description:	
Subjects received 1 injection of MenC-CRM vaccine, lyophilized formulation produced with drug substance manufactured at Emeryville, USA	
Arm type	Active comparator
Investigational medicinal product name	Meningococcal C-CRM conjugated
Investigational medicinal product code	MenC-CRM EMV
Other name	
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
1 single dose 0.5 mL per injection	
Arm title	MenC-CRM ROS_EMV
Arm description:	
Subjects enrolled to receive MenC-CRM ROS, but were mistakenly administered 1 injection of MenC-CRM EMV	
Arm type	administered mistakenly
Investigational medicinal product name	Meningococcal C-CRM conjugated
Investigational medicinal product code	MenC-CRM EMV
Other name	
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
1 single dose 0.5 mL per injection. Note: a different lot was used than in the MenC-CRM EMV arm.	

Number of subjects in period 1	MenC-CRM LIQ	MenC-CRM ROS	MenC-CRM EMV
Started	299	268	306
Completed	296	266	304
Not completed	3	2	2
Consent withdrawn by subject	1	-	2
Lost to follow-up	1	1	-
Protocol deviation	1	1	-

Number of subjects in period 1	MenC-CRM ROS_EMV
Started	119
Completed	119
Not completed	0
Consent withdrawn by subject	-
Lost to follow-up	-
Protocol deviation	-

Baseline characteristics

Reporting groups	
Reporting group title	MenC-CRM LIQ
Reporting group description:	
Subjects received 1 injection of MenC-CRM vaccine, liquid formulation	
Reporting group title	MenC-CRM ROS
Reporting group description:	
Subjects received 1 injection of MenC-CRM vaccine, lyophilized formulation produced with drug substance manufactured at Rosia, Italy	
Reporting group title	MenC-CRM EMV
Reporting group description:	
Subjects received 1 injection of MenC-CRM vaccine, lyophilized formulation produced with drug substance manufactured at Emeryville, USA	
Reporting group title	MenC-CRM ROS_EMV
Reporting group description:	
Subjects enrolled to receive MenC-CRM ROS, but were mistakenly administered 1 injection of MenC-CRM EMV	

Reporting group values	MenC-CRM LIQ	MenC-CRM ROS	MenC-CRM EMV
Number of subjects	299	268	306
Age categorical			
Units: Subjects			
Age continuous			
Units: months			
arithmetic mean	16.4	16.2	16.7
standard deviation	± 3.4	± 3.2	± 3.4
Gender categorical			
Units: Subjects			
Female	143	131	141
Male	156	137	165

Reporting group values	MenC-CRM ROS_EMV	Total	
Number of subjects	119	992	
Age categorical			
Units: Subjects			
Age continuous			
Units: months			
arithmetic mean	17.2		
standard deviation	± 3.3	-	
Gender categorical			
Units: Subjects			
Female	50	465	
Male	69	527	

End points

End points reporting groups

Reporting group title	MenC-CRM LIQ
Reporting group description:	
Subjects received 1 injection of MenC-CRM vaccine, liquid formulation	
Reporting group title	MenC-CRM ROS
Reporting group description:	
Subjects received 1 injection of MenC-CRM vaccine, lyophilized formulation produced with drug substance manufactured at Rosia, Italy	
Reporting group title	MenC-CRM EMV
Reporting group description:	
Subjects received 1 injection of MenC-CRM vaccine, lyophilized formulation produced with drug substance manufactured at Emeryville, USA	
Reporting group title	MenC-CRM ROS_EMV
Reporting group description:	
Subjects enrolled to receive MenC-CRM ROS, but were mistakenly administered 1 injection of MenC-CRM EMV	
Subject analysis set title	Enrolled Set
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All subjects who had signed an informed consent, undergone screening procedure(s) and were randomized.	
Subject analysis set title	Per Protocol Set
Subject analysis set type	Per protocol
Subject analysis set description:	
All subjects who signed an informed consent form, underwent screening procedure(s),were randomized, actually received a study vaccination, provided at least one evaluable serum sample, correctly received the vaccine, provided evaluable serum samples at the relevant time points (for subjects in the immunogenicity subset), and had no major protocol violation as defined prior to unblinding.	
Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects who signed an informed consent form, underwent screening procedure(s), were randomized and provided post vaccination safety data.	

Primary: Geometric Mean Human Serum Bactericidal Activity Titers Against N Meningitidis Serogroup C 28 Days After Vaccination

End point title	Geometric Mean Human Serum Bactericidal Activity Titers Against N Meningitidis Serogroup C 28 Days After Vaccination[1]
End point description:	
Immunogenicity was measured by human serum bactericidal activity (hSBA) geometric mean titers (GMTs) against N meningitidis type C, at day 29 after a single vaccination when administered to toddlers to assess the equivalence of MenC-CRM LIQ to MenC-CRM EMV and MenC-CRM ROS to MenC-CRM EMV.	
End point type	Primary
End point timeframe:	
1 month postvaccination (day 29)	

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis is associated to this Endpoint. Analyses were run descriptively.

End point values	MenC-CRM LIQ	MenC-CRM ROS	MenC-CRM EMV	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	283	259	281	
Units: Titers				
geometric mean (confidence interval 95%)				
Day 1	2.1 (2 to 2.2)	2.16 (2.05 to 2.26)	2.15 (2.05 to 2.25)	
Day 29	9.84 (8.39 to 12)	14 (12 to 16)	12 (10 to 14)	

Statistical analyses

Statistical analysis title	Equivalence of MenC-CRM liquid to MenC-CRM EMV

Statistical analysis description:

The study would be considered a success if the two-sided 95% confidence intervals (CIs) for the hSBA GMT ratios comparing MenC-CRM LIQ to MenC-CRM EMV at 28 days after a single vaccination were both within the equivalence interval (0.5, 2.0).

Comparison groups	MenC-CRM LIQ v MenC-CRM EMV
Number of subjects included in analysis	564
Analysis specification	Pre-specified
Analysis type	equivalence[2]
P-value	< 0.05 [3]
Method	ANOVA
Parameter estimate	hSBA GMT ratios
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	1

Notes:

[2] - The equivalence margin was (0.5, 2.0). If the two-sided 95% CI for the ratio of the hSBA GMTs at 28 days following vaccination was within this equivalence interval for each of the two coprimary comparisons, MenC-CRM LIQ and MenC-CRM EMV would be declared equivalent with respect to the immune response to the vaccines.
[3] - 95% CIs for the GMTs ratios were obtained by exponentiating difference of least square means of log10 transformed titers and both the limits of 95% CIs.

Statistical analysis title	Equivalence of MenC-CRM EMV to MenC-CRM ROS

Statistical analysis description:

The study would be considered a success if the two-sided 95% confidence intervals (CIs) for the hSBA GMT ratios comparing MenC-CRM LIQ to MenC-CRM EMV at 28 days after a single vaccination were both within the equivalence interval (0.5, 2.0).

Comparison groups	MenC-CRM EMV v MenC-CRM ROS
Number of subjects included in analysis	540
Analysis specification	Pre-specified
Analysis type	equivalence[4]
P-value	< 0.05 [5]
Method	ANOVA
Parameter estimate	hSBA GMT ratios
Point estimate	1.14

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	1.41

Notes:

[4] - The equivalence margin was (0.5, 2.0). If the two-sided 95% CI for the ratio of the hSBA GMTs at 28 days following vaccination was within this equivalence interval for each of the two coprimary comparisons, MenC-CRM LIQ and MenC-CRM EMV would be declared equivalent with respect to the immune response to the vaccines.

[5] - 95% CIs for the GMTs ratios were obtained by exponentiating difference of least square means of log10 transformed titers and both the limits of 95% CIs.

Secondary: Geometric Mean hSBA Titers Against N Meningitidis Serogroup C 28 Days After Vaccination

End point title	Geometric Mean hSBA Titers Against N Meningitidis Serogroup C 28 Days After Vaccination[6]

End point description:

Immunogenicity was measured by hSBA GMTs against N meningitidis type C, approximately 28 days (at day 29) after a single vaccination when administered to toddlers to assess the equivalence of MenC-CRM LIQ to MenC-CRM ROS.

End point type	Secondary

End point timeframe:

1 month postvaccination (day 29)

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analysis is associated to this Endpoint. Analyses were run descriptively.

End point values	MenC-CRM LIQ	MenC-CRM ROS		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	283	259		
Units: Titers				
geometric mean (confidence interval 95%)				
Day 1	2.1 (2 to 2.2)	2.16 (2.05 to 2.26)		
Day 29	9.84 (8.39 to 12)	14 (12 to 16)		

Statistical analyses

Statistical analysis title	Equivalence of MenC-CRM LIQ to MenC-CRM ROS

Statistical analysis description:

The secondary objective was to be assessed only if both primary objectives were met. Because of this, no adjustment for multiplicity was required. MenC-CRM liquid would be declared equivalent to MenC-CRM ROS if the two-sided 95% CI for the ratio of the hSBA GMTs at approximately 28 days following vaccination was within the equivalence interval (0.5, 2.0).

Comparison groups	MenC-CRM LIQ v MenC-CRM ROS

Number of subjects included in analysis	542
Analysis specification	Pre-specified
Analysis type	equivalence[7]
P-value	< 0.05 [8]
Method	ANOVA
Parameter estimate	Vaccine Group Ratios
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.58
upper limit	0.89

Notes:

[7] - The equivalence margin was (0.5, 2.0). If the two-sided 95% CI for the ratio of the hSBA GMTs at 28 days following vaccination was within this equivalence interval, the two vaccine groups would be declared equivalent with respect to the immune response to the vaccines.

[8] - 95% CIs for the GMTs ratios was obtained by exponentiating difference of least square means of log10 transformed titers and both the limits of 95% CIs

Secondary: Number Of Subjects Reporting Solicited Local And Systemic Adverse Events

End point title	Number Of Subjects Reporting Solicited Local And Systemic Adverse Events

End point description:

Safety was assessed as the number of subjects who reported solicited local and systemic adverse events following a single injection with either MenC-CRM LIQ or MenC-CRM ROS or MenC-CRM EMV. Safety was also assessed in subjects who mistakenly received MenC-CRM EMV instead of MenC-CRM ROS.

End point type	Secondary

End point timeframe:

From day 1 through day 7

End point values	MenC-CRM LIQ	MenC-CRM ROS	MenC-CRM EMV	MenC-CRM ROS_EMV
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	299	267	304	119
Units: Number of Subjects				
Any local	124	115	148	58
Injection site Tenderness	88	64	101	41
Injection site Erythema	222	200	211	81
Injection site Induration	252	227	236	88
Any systemic	163	140	155	60
Change in Eating habits	87	68	83	26
Sleepiness	66	55	56	24
Persistent Crying	45	41	36	15
Vomiting	9	11	7	4
Diarrhea	42	30	34	17
Irritability	101	76	87	32
Fever (≥38°C)	20	11	18	13

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited local and systemic adverse events from day 1 to 7. Serious adverse events (SAEs) and Unsolicited AEs (other than SAEs) from day 1 to day 29 (1 month after first vaccination).

Adverse event reporting additional description:

All Solicited AEs are classified as systematic assessment and all unsolicited AEs are classified as non-systematic assessment.
The total no. of subjects affected by non-serious adverse events refers to the total no. and percent of subjects with a non-serious AE that occurred at >5% in any group.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	15.1

Reporting groups

Reporting group title	MenC-CRM LIQ

Reporting group description:

Subjects received 1 injection of MenC-CRM vaccine, liquid formulation

Reporting group title	MenC-CRM ROS

Reporting group description:

Subjects received 1 injection of MenC-CRM vaccine, lyophilized formulation produced with drug substance manufactured at Rosia, Italy

Reporting group title	MenC-CRM EMV

Reporting group description:

Subjects received 1 injection of MenC-CRM vaccine, lyophilized formulation produced with drug substance manufactured at Emeryville, USA

Reporting group title	MenC-CRM ROS_EMV

Reporting group description:

Subjects enrolled to receive MenC-CRM ROS, but were mistakenly administered 1 injection of MenC-CRM EMV

Serious adverse events	MenC-CRM LIQ	MenC-CRM ROS	MenC-CRM EMV
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 299 (0.00%)	3 / 267 (1.12%)	2 / 304 (0.66%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Gastrointestinal disorders			
Diarrhea			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 299 (0.00%)	0 / 267 (0.00%)	1 / 304 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			

alternative assessment type: Systematic			
subjects affected / exposed	0 / 299 (0.00%)	0 / 267 (0.00%)	1 / 304 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis rotavirus			
subjects affected / exposed	0 / 299 (0.00%)	2 / 267 (0.75%)	0 / 304 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 299 (0.00%)	1 / 267 (0.37%)	1 / 304 (0.33%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	MenC-CRM ROS_EMV		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 119 (0.84%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Gastrointestinal disorders			
Diarrhea			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 119 (0.84%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Gastroenteritis rotavirus			
subjects affected / exposed	0 / 119 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Pneumonia			
subjects affected / exposed	0 / 119 (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	MenC-CRM LIQ	MenC-CRM ROS	MenC-CRM EMV
Total subjects affected by non-serious adverse events			
subjects affected / exposed	196 / 299 (65.55%)	178 / 267 (66.67%)	206 / 304 (67.76%)
Nervous system disorders			
Somnolence			
subjects affected / exposed	66 / 299 (22.07%)	55 / 267 (20.60%)	56 / 304 (18.42%)
occurrences (all)	71	59	61
General disorders and administration site conditions			
Crying			
alternative assessment type: Systematic			
subjects affected / exposed	45 / 299 (15.05%)	41 / 267 (15.36%)	36 / 304 (11.84%)
occurrences (all)	50	43	40
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed	77 / 299 (25.75%)	67 / 267 (25.09%)	93 / 304 (30.59%)
occurrences (all)	79	68	95
Injection site induration			
subjects affected / exposed	47 / 299 (15.72%)	40 / 267 (14.98%)	68 / 304 (22.37%)
occurrences (all)	48	40	70
Injection site pain			
alternative assessment type: Systematic			
subjects affected / exposed	88 / 299 (29.43%)	64 / 267 (23.97%)	101 / 304 (33.22%)
occurrences (all)	91	64	103
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed	101 / 299 (33.78%)	76 / 267 (28.46%)	87 / 304 (28.62%)
occurrences (all)	122	91	103
Pyrexia			

subjects affected / exposed	27 / 299 (9.03%)	15 / 267 (5.62%)	23 / 304 (7.57%)
occurrences (all)	32	17	25
Gastrointestinal disorders			
Diarrhoea			
alternative assessment type: Systematic			
subjects affected / exposed	44 / 299 (14.72%)	32 / 267 (11.99%)	36 / 304 (11.84%)
occurrences (all)	59	39	43
Psychiatric disorders			
Eating disorder			
subjects affected / exposed	88 / 299 (29.43%)	68 / 267 (25.47%)	83 / 304 (27.30%)
occurrences (all)	106	84	92
Infections and infestations			
Respiratory tract infection			
subjects affected / exposed	10 / 299 (3.34%)	7 / 267 (2.62%)	12 / 304 (3.95%)
occurrences (all)	10	7	12

Non-serious adverse events	MenC-CRM ROS_EMV		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	79 / 119 (66.39%)		
Nervous system disorders			
Somnolence			
subjects affected / exposed	24 / 119 (20.17%)		
occurrences (all)	26		
General disorders and administration site conditions			
Crying			
alternative assessment type: Systematic			
subjects affected / exposed	15 / 119 (12.61%)		
occurrences (all)	20		
Injection site erythema			
alternative assessment type: Systematic			
subjects affected / exposed	38 / 119 (31.93%)		
occurrences (all)	39		
Injection site induration			
subjects affected / exposed	31 / 119 (26.05%)		
occurrences (all)	32		
Injection site pain			
alternative assessment type:			

Systematic			
subjects affected / exposed	41 / 119 (34.45%)		
occurrences (all)	42		
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed	32 / 119 (26.89%)		
occurrences (all)	35		
Pyrexia			
subjects affected / exposed	17 / 119 (14.29%)		
occurrences (all)	22		
Gastrointestinal disorders			
Diarrhoea			
alternative assessment type: Systematic			
subjects affected / exposed	17 / 119 (14.29%)		
occurrences (all)	19		
Psychiatric disorders			
Eating disorder			
subjects affected / exposed	26 / 119 (21.85%)		
occurrences (all)	31		
Infections and infestations			
Respiratory tract infection			
subjects affected / exposed	6 / 119 (5.04%)		
occurrences (all)	6		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 January 2012	Amendment 1 issued dealt with changes to the randomization ratio and sample size.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
22 May 2011	There was an unplanned interruption to subject enrollment due to the identification of the erroneously dispatched vaccine lot.	13 August 2012

Notes:

Limitations and caveats

None reported