Clinical trial results:
A Phase 3, Multi-center, Open-label Study to Evaluate Immunogenicity and Safety of Novartis Meningococcal ACWY Conjugate Vaccine (MenACWY-CRM) in Healthy Children, Adolescents and Adults in Russia

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

Summary

EudraCT number	2014-004617-82
Trial protocol	Outside EU/EEA
Global end of trial date	19 March 2013

Results information

Result version number	v2 (current)
This version publication date	16 June 2016
First version publication date	08 January 2015
Version creation reason	• Correction of full data set e-QC of the study needed because of EudraCT system glitch and updates are required.

Trial information

Trial identification

Sponsor protocol code	V59_50

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01725217
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Vaccines and Diagnostics SRL
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	13 September 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 March 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the immunogenicity of a single injection of MenACWY-CRM vaccine as measured by the percentage of subjects with human serum bactericidal assay (hSBA)seroresponse, directed against N meningitidis serogroups A, C, W, and Y.

Protection of trial subjects:

Standard immunization practices were observed and care was taken to administer the injection intramuscularly. As with all injectable vaccines, appropriate medical treatment and supervision were readily available in case of anaphylactic reactions following administration of the study vaccine. Epinephrine 1:1000 and diphenhydramine, or locally approved medications were available in case of any anaphylactic reactions.
This clinical study was designed and implemented and reported in accordance with the ICH (International Conference on Harmozination) Harmonized Tripartite Guidelines for Good Clinical Practice (GCP), with applicable local regulations and with the ethical principles laid down in the Declaration of Helsinki.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 November 2012
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	Russian Federation: 198
Worldwide total number of subjects	198
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)	76
Adolescents (12-17 years)	56

Adults (18-64 years)	63
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited from 4 centres in Russia.

Pre-assignment

Screening details:

All subjects were enrolled in the trial.

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?	No
Arm title	≥2 to ≤10 Years

Arm description:

Subjects ≥2 to ≤10 years of age who received one vaccination of MenACWY-CRM

Arm type	Experimental
Investigational medicinal product name	Meningococcal (groups A, C, W, and Y) oligosaccharide diphtheria CRM-197
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose 0.5 mL of injectable solution was administered intramuscularly

Arm title	≥11 to ≤17 Years

Arm description:

Subjects ≥11 to ≤17 years of age who received one vaccination of MenACWY-CRM

Arm type	Experimental
Investigational medicinal product name	Meningococcal (groups A, C, W, and Y) oligosaccharide diphtheria CRM-197
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose 0.5 mL of injectable solution was administered intramuscularly

Arm title	≥18 years

Arm description:

Subjects ≥18 years of age who received one vaccination of MenACWY-CRM

Arm type	Experimental

Investigational medicinal product name	Meningococcal (groups A, C, W, and Y) oligosaccharide diphtheria CRM-197
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose 0.5 mL of injectable solution was administered intramuscularly

Arm title	Overall (≥2 years)

Arm description:

All subjects ≥2 years of age who received one vaccination of MenACWY-CRM

Arm type	Experimental
Investigational medicinal product name	Meningococcal (groups A, C, W, and Y) oligosaccharide diphtheria CRM-197
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose 0.5 mL of injectable solution was administered intramuscularly

Number of subjects in period 1	≥2 to ≤10 Years	≥11 to ≤17 Years	≥18 years
Started	66	66	66
Completed	65	66	66
Not completed	1	0	0
Consent withdrawn by subject	1	-	-

Number of subjects in period 1	Overall (≥2 years)
Started	198
Completed	197
Not completed	1
Consent withdrawn by subject	1

Baseline characteristics

Reporting groups	
Reporting group title	≥2 to ≤10 Years
Reporting group description:	
Subjects ≥2 to ≤10 years of age who received one vaccination of MenACWY-CRM	

Reporting group title	≥11 to ≤17 Years
Reporting group description:	
Subjects ≥11 to ≤17 years of age who received one vaccination of MenACWY-CRM	

Reporting group title	≥18 years
Reporting group description:	
Subjects ≥18 years of age who received one vaccination of MenACWY-CRM	

Reporting group title	Overall (≥2 years)
Reporting group description:	
All subjects ≥2 years of age who received one vaccination of MenACWY-CRM	

Reporting group values	≥2 to ≤10 Years	≥11 to ≤17 Years	≥18 years
Number of subjects	66	66	66
Age categorical Units: Subjects			
Age continuous			
Analysis was done on the all enrolled set			
Units: years			
arithmetic mean	6	13.8	38.8
standard deviation	± 2.7	± 2.1	± 12.5
Gender categorical			
Analysis was done on the all enrolled set			
Units: Subjects			
Female	35	29	44
Male	31	37	22

Reporting group values	Overall (≥2 years)	Total	
Number of subjects	198	198	
Age categorical Units: Subjects			
Age continuous			
Analysis was done on the all enrolled set			
Units: years			
arithmetic mean	19.6		
standard deviation	± 15.9	-	
Gender categorical			
Analysis was done on the all enrolled set			
Units: Subjects			
Female	108	108	
Male	90	90	

End points

End points reporting groups

Reporting group title	≥2 to ≤10 Years
Reporting group description:	
Subjects ≥2 to ≤10 years of age who received one vaccination of MenACWY-CRM	
Reporting group title	≥11 to ≤17 Years
Reporting group description:	
Subjects ≥11 to ≤17 years of age who received one vaccination of MenACWY-CRM	
Reporting group title	≥18 years
Reporting group description:	
Subjects ≥18 years of age who received one vaccination of MenACWY-CRM	
Reporting group title	Overall (≥2 years)
Reporting group description:	
All subjects ≥2 years of age who received one vaccination of MenACWY-CRM	
Subject analysis set title	All enrolled Set
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All subjects who have signed an informed consent, undergone screening procedure(s), and have a subject number assigned.	
Subject analysis set title	Full Analysis Set (FAS)
Subject analysis set type	Full analysis
Subject analysis set description:	
All subjects in the exposed population who provided evaluable serum samples whose assay results are available for at least one serogroup on day 1 and/or day 29	
Subject analysis set title	Exposed Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All enrolled subjects who actually received study vaccination	
Subject analysis set title	Safety Set (>2 - <3 years of age)
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects in the exposed population between 2 and 3 years of age who provided any post-baseline safety data	
Subject analysis set title	Safety Set (>2 - <5 years of age)
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects in the exposed population between 2 and 5 years of age who provided any post-baseline safety data	
Subject analysis set title	Safety Set (>2 years of age)
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects in the exposed population who provided any post-baseline safety data	
Subject analysis set title	Safety Set (>6 - <10 years of age)
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects in the exposed population between 6 and 10 years of age who provided any post-baseline safety data	
Subject analysis set title	Safety Set (>6 years of age)

Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects in the exposed population older than 6 years of age who provided any post-baseline safety data

Primary: 1) Percentages of Overall Subjects With Seroresponse After MenACWY-CRM Vaccination

End point title	1) Percentages of Overall Subjects With Seroresponse After MenACWY-CRM Vaccination[1][2]

End point description:

Immunogenicity was measured as the percentages of overall subjects with hSBA seroresponse, directed against N. meningitidis serogroups A, C, W and Y, evaluated by serum bactericidal assay using human complement (hSBA), 28 days after one vaccination of MenACWY-CRM (day 29).
The seroresponse is defined as the percentages of subjects achieving hSBA ≥1:8 postvaccination with a prevaccination hSBA <1:4 and the percentages of subjects achieving at least four-fold increases in hSBA from day 1 in subjects with a baseline hSBA ≥1:4.
Analysis was done on Full Analysis Set (FAS).

End point type	Primary

End point timeframe:

Day 29

Notes:

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

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: there was no statistical analysis for this endpoint.

End point values	Overall (≥2 years)			
Subject group type	Reporting group			
Number of subjects analysed	193[3]			
Units: Percentages of Subjects				
number (confidence interval 95%)				
Men A	85 (79 to 90)			
Men C	74 (67 to 80)			
Men W	60 (53 to 67)			
Men Y	83 (77 to 88)			

Notes:

[3] - Men C, N= 192
Men W, N=192
Men Y, N= 191

Statistical analyses

No statistical analyses for this end point

Secondary: 2) Percentages of Subjects With Seroresponse After MenACWY-CRM Vaccination, by Age Group

End point title	2) Percentages of Subjects With Seroresponse After MenACWY-CRM Vaccination, by Age Group[4]

End point description:

Immunogenicity was measured as the percentages of subjects stratified by age group with hSBA response, directed against N. meningitidis serogroups A, C, W and Y, 28 days after one vaccination of MenACWY-CRM.
Analysis was done on the FAS.

End point type	Secondary

End point timeframe:

Day 29

Notes:

[4] - 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: there was no statistical analysis for this endpoint.

End point values	≥2 to ≤10 Years	≥11 to ≤17 Years	≥18 years	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	63[5]	65	65	
Units: Percentages of Subjects				
number (confidence interval 95%)				
Men A	89 (78 to 95)	89 (79 to 96)	77 (65 to 86)	
Men C	69 (56 to 80)	82 (70 to 90)	71 (58 to 81)	
Men W	73 (60 to 83)	51 (38 to 63)	57 (44 to 69)	
Men Y	77 (65 to 87)	88 (77 to 95)	85 (74 to 92)	

Notes:

[5] - Men C, N= 62,65,65
Men W, N= 62,65,65
Men Y, N= 61,65,65

Statistical analyses

No statistical analyses for this end point

Secondary: 3) Geometric Mean Titers (GMTs) of Subjects at Baseline and After MenACWY-CRM Vaccination

End point title	3) Geometric Mean Titers (GMTs) of Subjects at Baseline and After MenACWY-CRM Vaccination

End point description:

Immunogenicity was measured as hSBA GMTs, against N. meningitidis serogroups A, C, W and Y, at baseline (day 1) and 28 days after MenACWY-CRM vaccination (day 29), overall and by age group. Analysis was done on the FAS.

End point type	Secondary

End point timeframe:

Day 29

End point values	≥2 to ≤10 Years	≥11 to ≤17 Years	≥18 years	Overall (≥2 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	63[6]	65	65	193
Units: Titers				
geometric mean (confidence interval 95%)				
Men A (Day 1)	2.17 (1.79 to 2.62)	2.43 (2.01 to 2.93)	2.61 (2.11 to 3.23)	2.35 (2.17 to 2.55)
Men A (Day 29)	67 (38 to 119)	134 (77 to 233)	76 (41 to 143)	93 (73 to 119)
Men C (Day 1)	3.16 (2.18 to 4.57)	3.59 (2.5 to 5.15)	6.68 (4.43 to 10)	4.07 (3.45 to 4.8)
Men C (Day 29)	28 (14 to 56)	47 (24 to 92)	112 (52 to 243)	59 (43 to 81)

Men W (Day 1)	7.93 (4.69 to 13)	21 (13 to 36)	13 (7.16 to 23)	12 (9.42 to 15)
Men W (Day 29)	94 (56 to 155)	117 (72 to 191)	143 (83 to 248)	111 (89 to 139)
Men Y (Day 1)	3.02 (2.33 to 3.92)	3.73 (2.89 to 4.82)	2.74 (2.05 to 3.66)	2.93 (2.61 to 3.28)
Men Y (Day 29)	32 (18 to 56)	67 (39 to 115)	80 (43 to 147)	58 (46 to 74)

Notes:

[6] - Men C (Day 29), N=62,65,65,192
Men C (Day 29), N=62,65,65,192

Statistical analyses

No statistical analyses for this end point

Secondary: 4) Percentages of Subjects With hSBA Titer ≥1:8 at Baseline and After MenACWY-CRM Vaccination

End point title	4) Percentages of Subjects With hSBA Titer ≥1:8 at Baseline and After MenACWY-CRM Vaccination

End point description:

Immunogenicity was measured as the percentages of subjects with hSBA titer ≥1:8, at baseline (day 1) and 28 days after MenACWY-CRM vaccination (day 29), overall and bye age group.
Analysis was done on the FAS.

End point type	Secondary

End point timeframe:

Days 1 and 29

End point values	≥2 to ≤10 Years	≥11 to ≤17 Years	≥18 years	Overall (≥2 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	63[7]	65	65	193
Units: Percentages of Subjects				
number (confidence interval 95%)				
Men A (Day 1)	2 (0.04 to 9)	5 (1 to 13)	11 (4 to 21)	6 (3 to 10)
Men A (Day 29)	89 (78 to 95)	92 (83 to 97)	85 (74 to 92)	89 (83 to 93)
Men C (Day 1)	13 (6 to 23)	17 (9 to 28)	49 (37 to 62)	26 (20 to 33)
Men C (Day 29)	76 (63 to 86)	86 (75 to 93)	89 (79 to 96)	84 (78 to 89)
Men W (Day 1)	30 (19 to 43)	71 (58 to 81)	69 (57 to 80)	57 (50 to 64)
Men W (Day 29)	95 (87 to 99)	98 (92 to 100)	97 (89 to 100)	97 (93 to 99)
Men Y (Day 1)	10 (4 to 20)	15 (8 to 26)	22 (12 to 33)	16 (11 to 22)
Men Y (Day 29)	79 (67 to 88)	94 (85 to 98)	89 (79 to 96)	88 (82 to 92)

Notes:

[7] - Day29
Men C,N=62,65,65,192
Men W,N=62,65,65,192
Men Y,N=62,65,65,192
Day 1
MenY,N= 62,65,65,192

Statistical analyses

No statistical analyses for this end point

Secondary: 5) Percentages of Subjects Reporting Solicited local and systemic Adverse Events (AEs) After MenACWY-CRM Vaccination

End point title	5) Percentages of Subjects Reporting Solicited local and systemic Adverse Events (AEs) After MenACWY-CRM Vaccination

End point description:

Safety was assessed in terms of percentages of subjects who reported solicited local and systemic Adverse Events (AEs) after MenACWY-CRM vaccination, overall and by age group.
Analysis was done on safety set

End point type	Secondary

End point timeframe:

Within days 1 through 7 postvaccination

End point values	Safety Set (>2 - <3 years of age)	Safety Set (>2 - <5 years of age)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	18	27		
Units: Percentages of Subjects				
number (not applicable)				
Tenderness	7	11		
Erythema	5	7		
Induration	3	5		
Change in Eating Habits	1	1		
Sleepiness	5	9		
Irritability	3	7		
Vomiting	0	1		
Diarrhea	2	3		
Rash	1	1		
Fever (≥38 °C)	1	1		
Use of analgesic/antipyretics	0	2		

Statistical analyses

No statistical analyses for this end point

Secondary: 6) Percentages of Subjects Reporting Solicited local and systemic Adverse Events (AEs) After MenACWY-CRM Vaccination

End point title	6) Percentages of Subjects Reporting Solicited local and systemic Adverse Events (AEs) After MenACWY-CRM Vaccination[8]

End point description:

Safety was assessed in terms of percentages of subjects who reported solicited local and systemic Adverse Events (AEs) after MenACWY-CRM vaccination, overall and by age group.
Analysis was done on safety set.

End point type	Secondary

End point timeframe:

Within days 1 through 7 postvaccination

Notes:

[8] - 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: there was no statistical analysis for this endpoint.

End point values	≥11 to ≤17 Years	≥18 years	Safety Set (>6 - <10 years of age)	Safety Set (>6 years of age)
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	66	66	38	170
Units: Percentages of Subjects				
number (not applicable)				
Pain	33	33	16	82
Erythema	12	11	7	30
Induration	11	8	4	23
Chills	5	8	3	16
Nausea	7	5	1	13
Malaise	15	13	6	34
Myalgia	11	9	5	33
Arthralgia	7	7	1	15
Headache	18	18	7	43
Rash	0	3	1	4
Fever (≥38 °C)	2	1	2	5
Use of analgesic/antipyretics	6	6	7	19

Statistical analyses

No statistical analyses for this end point

Secondary: 7) Percentages of Subjects Reporting Unsolicited Adverse Events (AEs) After MenACWY-CRM Vaccination

End point title	7) Percentages of Subjects Reporting Unsolicited Adverse Events (AEs) After MenACWY-CRM Vaccination

End point description:

Safety was assessed in terms of percentages of subjects who reported all the adverse events (AEs) occurring from day 1 through 7, medically attended AEs,SAEs and AEs resulting in premature withdrawal, from day 1 through 29, after MenACWY-CRM vaccination, overall and by age group. Analysis was done on safety set.

End point type	Secondary

End point timeframe:

AEs occurring from day 1 through 7, medically attended AEs, SAEs and AEs resulting in premature withdrawal, from day 1 through 29

End point values	≥2 to ≤10 Years	≥11 to ≤17 Years	≥18 years	Overall (≥2 years)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	65	66	66	197
Units: Percentages of Subjects				
number (not applicable)				
Any AEs (days 1 through 7)	13	8	12	33
At least possibly related AEs (days 1 through 7)	2	6	12	20
Any SAE (days 1 through 29)	0	0	0	0
At least possibly related SAE (days 1 through 29)	0	0	0	0
Medically attended AE (days 1 through 29)	5	1	2	8
Premature withdrawal due to AE (days 1 through 29)	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From day 1 through day 29	
Adverse event reporting additional description:	
Solicited local and systemic AEs were collected within days 1 through 7 postvaccination. All unsolicited AEs from days 1 through 7, SAEs from days 1 through 29.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups	
Reporting group title	≥2 to ≤10 Years
Reporting group description:	
Subjects ≥2 to ≤10 years of age who received one vaccination of MenACWY-CRM	
Reporting group title	≥11 to ≤17 Years
Reporting group description:	
Subjects ≥11 to ≤17 years of age who received one vaccination of MenACWY-CRM	
Reporting group title	≥18 years
Reporting group description:	
Subjects ≥18 years of age who received one vaccination of MenACWY-CRM	
Reporting group title	Overall (≥2 years)
Reporting group description:	
All subjects ≥2 years of age who received one vaccination of MenACWY-CRM	

Serious adverse events	≥2 to ≤10 Years	≥11 to ≤17 Years	≥18 years
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 65 (0.00%)	0 / 66 (0.00%)	0 / 66 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Overall (≥2 years)		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 197 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	≥2 to ≤10 Years	≥11 to ≤17 Years	≥18 years
Total subjects affected by non-serious adverse events			
subjects affected / exposed	42 / 65 (64.62%)	42 / 66 (63.64%)	44 / 66 (66.67%)
Nervous system disorders			
Headache			
subjects affected / exposed	8 / 65 (12.31%)	18 / 66 (27.27%)	18 / 66 (27.27%)
occurrences (all)	10	21	19
Somnolence			
subjects affected / exposed	9 / 65 (13.85%)	1 / 66 (1.52%)	0 / 66 (0.00%)
occurrences (all)	9	1	0
General disorders and administration site conditions			
Chills			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 65 (4.62%)	5 / 66 (7.58%)	8 / 66 (12.12%)
occurrences (all)	3	6	8
Injection site erythema			
subjects affected / exposed	12 / 65 (18.46%)	13 / 66 (19.70%)	10 / 66 (15.15%)
occurrences (all)	13	14	13
Injection site induration			
subjects affected / exposed	8 / 65 (12.31%)	11 / 66 (16.67%)	8 / 66 (12.12%)
occurrences (all)	9	12	10
Injection site pain			
subjects affected / exposed	27 / 65 (41.54%)	33 / 66 (50.00%)	33 / 66 (50.00%)
occurrences (all)	28	35	35
Malaise			
subjects affected / exposed	6 / 65 (9.23%)	15 / 66 (22.73%)	13 / 66 (19.70%)
occurrences (all)	7	17	15
Gastrointestinal disorders			
Nausea			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 65 (1.54%)	7 / 66 (10.61%)	5 / 66 (7.58%)
occurrences (all)	2	7	5
Psychiatric disorders			
Irritability			
subjects affected / exposed	7 / 65 (10.77%)	0 / 66 (0.00%)	0 / 66 (0.00%)
occurrences (all)	7	0	0
Musculoskeletal and connective tissue			

disorders			
Arthralgia			
subjects affected / exposed	1 / 65 (1.54%)	7 / 66 (10.61%)	7 / 66 (10.61%)
occurrences (all)	1	8	7
Myalgia			
subjects affected / exposed	5 / 65 (7.69%)	19 / 66 (28.79%)	9 / 66 (13.64%)
occurrences (all)	5	20	9
Infections and infestations			
Rhinitis			
subjects affected / exposed	6 / 65 (9.23%)	0 / 66 (0.00%)	1 / 66 (1.52%)
occurrences (all)	6	0	1

Non-serious adverse events	Overall (≥2 years)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	128 / 197 (64.97%)		
Nervous system disorders			
Headache			
subjects affected / exposed	44 / 197 (22.34%)		
occurrences (all)	50		
Somnolence			
subjects affected / exposed	10 / 197 (5.08%)		
occurrences (all)	10		
General disorders and administration site conditions			
Chills			
alternative assessment type: Non-systematic			
subjects affected / exposed	16 / 197 (8.12%)		
occurrences (all)	17		
Injection site erythema			
subjects affected / exposed	35 / 197 (17.77%)		
occurrences (all)	40		
Injection site induration			
subjects affected / exposed	27 / 197 (13.71%)		
occurrences (all)	31		
Injection site pain			
subjects affected / exposed	93 / 197 (47.21%)		
occurrences (all)	98		
Malaise			

subjects affected / exposed occurrences (all)	34 / 197 (17.26%) 39		
Gastrointestinal disorders Nausea alternative assessment type: Non-systematic subjects affected / exposed occurrences (all)	 13 / 197 (6.60%) 14		
Psychiatric disorders Irritability subjects affected / exposed occurrences (all)	 7 / 197 (3.55%) 7		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Myalgia subjects affected / exposed occurrences (all)	 15 / 197 (7.61%) 16 33 / 197 (16.75%) 34		
Infections and infestations Rhinitis subjects affected / exposed occurrences (all)	 7 / 197 (3.55%) 7		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 June 2012	Indicate the number of children aged 2-3 y.o within the group of 66 children aged 2-10 y.o.; state vaccination timeframe in the section "Methodology"; state that the interval between blood draw is the same for all vaccinated subjects; list all contraindications listed in the annotation for use in the exclusion criteria; exclude possibility of IMP use which was stored in terms of temperature deviations; indicate the difference of systemic reactions amongst different age groups.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported