Clinical trial results:
A Phase 3, Randomized, Comparative, Multicenter Observer-Blind Study Evaluating the Safety and Immunogenicity of Novartis rMenB+OMV NZ Vaccine Formulated with Outer Membrane Vesicle (OMV) Manufactured at Two Different Sites, in Healthy Adolescents Aged 11-17 Years

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

Summary

EudraCT number	2014-004476-30
Trial protocol	Outside EU/EEA
Global end of trial date	01 December 2011

Results information

Result version number	v2 (current)
This version publication date	03 June 2016
First version publication date	26 December 2014
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	V72_41

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01423084
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 and Diagnostics SRL, RegistryContactVaccinesUS@novartis.com
Scientific contact	Posting Director, Novartis Vaccines and Diagnostics SRL, 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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 March 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 December 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the equivalence of rMenB+OMV NZ lot 1 to rMenB+OMV NZ lot 2 when administered to adolescents, as measured by human serum bactericidal activity (hSBA) geometric mean titers (GMTs) against 3 N. meningitidis serogroup B reference strains (H44/76, 5/99, and NZ98/254) and as measured by Enzymelinked immunosorbent assay (ELISA) geometric mean concentrations (GMCs) against vaccine antigen 287-953, approximately 30 days after a primary vaccination course of two doses administered one month apart.

Protection of trial subjects:

This clinical study was designed, conducted and reported in accordance with the International Conference on Harmonization (ICH) Harmonized Tripartite Guidelines for 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), with the ethical principles laid down in the Declaration of Helsinki, and with the applicable regulatory requirement(s) for the country in which the trial was conducted. Specifically, this trial was conducted under a protocol reviewed and approved by an EC; the trial was conducted by scientifically and medically qualified persons; the benefits of the study are in percentage to the risks; the rights and welfare of the subjects were respected; the physicians conducting the trial did not find the hazards to outweigh the potential benefits; each subject, or where applicable, each subject's legally acceptable representative(s) gave his or her written informed consent before any protocol-driven tests or evaluations were performed. A copy of the ICH GCP guidelines and of the Declaration of Helsinki was included in the investigator's study file.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 August 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	Australia: 75
Country: Number of subjects enrolled	Canada: 269
Worldwide total number of subjects	344
EEA total number of subjects	0

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)	0
Children (2-11 years)	48
Adolescents (12-17 years)	296
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 7 centres in Canada and 6 in Australia

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	Double blind
Roles blinded	Investigator, Monitor, Data analyst, Carer, Assessor, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	4CMenB_Rosia

Arm description:

Subjects received two doses of rMenB+OMV NZ vaccine from lot 1 manufactured at Rosia facility.

Arm type	Experimental
Investigational medicinal product name	rMenB+OMV NZ
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received two injections of 0.5 mL dose administered intra-muscularly (IM) into the deltoid area.

Arm title	4CMenB_Siena

Arm description:

Subjects received two doses of rMenB+OMV NZ vaccinations from lot 2 manufactured at Siena facility.

Arm type	Experimental
Investigational medicinal product name	rMenB+OMV NZ
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received two injections of 0.5 mL dose administered intra-muscularly (IM) into the deltoid area.

Number of subjects in period 1	4CMenB_Rosia	4CMenB_Siena
Started	170	174
Completed	168	170
Not completed	2	4
Consent withdrawn by subject	2	3
Adverse event, non-fatal	-	1

Baseline characteristics

Reporting groups	
Reporting group title	4CMenB_Rosia
Reporting group description:	
Subjects received two doses of rMenB+OMV NZ vaccine from lot 1 manufactured at Rosia facility.	
Reporting group title	4CMenB_Siena
Reporting group description:	
Subjects received two doses of rMenB+OMV NZ vaccinations from lot 2 manufactured at Siena facility.	

Reporting group values	4CMenB_Rosia	4CMenB_Siena	Total
Number of subjects	170	174	344
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	13.6	13.8	
standard deviation	± 1.9	± 1.8	-
Gender categorical Units: Subjects			
Female	72	82	154
Male	98	92	190

End points

End points reporting groups

Reporting group title	4CMenB_Rosia
Reporting group description:	
Subjects received two doses of rMenB+OMV NZ vaccine from lot 1 manufactured at Rosia facility.	
Reporting group title	4CMenB_Siena
Reporting group description:	
Subjects received two doses of rMenB+OMV NZ vaccinations from lot 2 manufactured at Siena facility.	
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 were randomized.	

Subject analysis set title	All Exposed Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All enrolled subjects who actually received a study vaccination.	
Subject analysis set title	Safety Set
Subject analysis set type	Safety analysis
Subject analysis set description:	
All subjects in the Exposed population who provided post vaccination safety data	
Subject analysis set title	Per Protocol Set
Subject analysis set type	Per protocol
Subject analysis set description:	
All subjects in the Enrolled Set who correctly received the vaccine, provided evaluable serum samples at the relevant time points and had no major protocol violation as defined prior to un-blinding.	

Primary: 1) Human Serum Bactericidal Activity (hSBA) Geometric Mean Titers (GMTs) against 3 Neisseria.meningitidis (N. meningitidis) serogroup B reference strains.

End point title	1) Human Serum Bactericidal Activity (hSBA) Geometric Mean Titers (GMTs) against 3 Neisseria.meningitidis (N. meningitidis) serogroup B reference strains.
End point description:	
Two different lots of rMenB+OMV NZ are evaluated in terms of hSBA GMTs against 3 different strains of serogroup B N. meningitidis antigens.	
End point type	Primary
End point timeframe:	
Day 61	

End point values	4CMenB_Rosia	4CMenB_Siena		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	147[1]	151[2]		
Units: Titers				
geometric mean (confidence interval 95%)				

H44/76 strain	111 (96 to 129)	111 (96 to 128)		
NZ98/254 strain	9.27 (7.44 to 12)	11 (9.22 to 14)		
5/99 strain	183 (160 to 209)	199 (174 to 227)		

Notes:

[1] - Analysis was done on the Per Protocol Set.

[2] - Analysis was done on the Per Protocol Set.
For strain 5/99, N=152
Stat. Analysis N=299

Statistical analyses

Statistical analysis title	Equivalence of 2 differents lots of rMenB+OMV NZ
Statistical analysis description:	
Equivalence of 2 differents lots of rMenB+OMV NZ in terms of hSBA GMTs against H44/76 strain	
Comparison groups	4CMenB_Rosia v 4CMenB_Siena
Number of subjects included in analysis	298
Analysis specification	Pre-specified
Analysis type	equivalence[3]
Parameter estimate	between groups ratio
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.23

Notes:

[3] - Two different lots of rMenB+OMV NZ are to be considered equivalent in terms of hSBA GMTs against H44/76 strain if t the two sided 95% Confidence Interval (CI) of the between groups GMTs ratio at day 31 (ie, one month after the second vaccination) does not exceed the range 0.5 (lower limit) - 2.0 (higher limit).

Statistical analysis title	Equivalence of 2 differents lots of rMenB+OMV NZ
Statistical analysis description:	
Equivalence of 2 differents lots of rMenB+OMV NZ in terms of hSBA GMTs against NZ98/254 strain	
Comparison groups	4CMenB_Rosia v 4CMenB_Siena
Number of subjects included in analysis	298
Analysis specification	Pre-specified
Analysis type	equivalence[4]
Parameter estimate	between groups ratio
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	1.09

Notes:

[4] - Two different lots of rMenB+OMV NZ are to be considered equivalent in terms of hSBA GMTs against NZ 98/254 strain if t the two sided 95% Confidence Interval (CI) of the between groups GMTs ratio at day 31 (ie, one month after the second vaccination) does not exceed the range 0.5 (lower limit) - 2.0 (higher limit).

Statistical analysis title	Equivalence of 2 differents lots of rMenB+OMV NZ

Statistical analysis description:	
Equivalence of 2 differents lots of rMenB+OMV NZ in terms of hSBA GMTs against 5/99 strain	
Comparison groups	4CMenB_Rosia v 4CMenB_Siena
Number of subjects included in analysis	298
Analysis specification	Pre-specified
Analysis type	equivalence[5]
Parameter estimate	between groups ratio
Point estimate	0.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.1

Notes:

[5] - Two different lots of rMenB+OMV NZ are to be considered equivalent in terms of hSBA GMTs against 5/99 strain if the two sided 95% Confidence Interval (CI) of the between groups GMTs ratio at day 31 (ie, one month after the second vaccination) does not exceed the range 0.5 (lower limit) - 2.0 (higher limit).

Primary: 2) Enzyme-linked immunosorbent assay (ELISA) geometric mean concentrations (GMCs) against vaccine antigen 287-953

End point title	2) Enzyme-linked immunosorbent assay (ELISA) geometric mean concentrations (GMCs) against vaccine antigen 287-953

End point description:

The immune response of two different lots of rMenB+OMV NZ is evaluated in terms of ELISA GMCs against vaccine antigen 287-953.

End point type	Primary

End point timeframe:

Day 61

End point values	4CMenB_Rosia	4CMenB_Siena		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	147[6]	152[7]		
Units: IU/mL				
geometric mean (confidence interval 95%)	2729 (2338 to 3186)	3291 (2829 to 3828)		

Notes:

[6] - Analysis was done on the Per Protocol Set.

[7] - Analysis was done on the Per Protocol Set.

Statistical analyses

Statistical analysis title	Equivalence in terms of hSBA GMTs

Statistical analysis description:

Equivalence of 2 differents lots of rMenB+OMV NZ in terms of ELISA GMCs

Comparison groups	4CMenB_Rosia v 4CMenB_Siena

Number of subjects included in analysis	299
Analysis specification	Pre-specified
Analysis type	equivalence[8]
Parameter estimate	between groups ratio
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	1.02

Notes:

[8] - Two different lots of rMenB+OMV NZ are to be considered equivalent in terms of ELISA GMCs against vaccine antigen 287-953 if t the two sided 95% Confidence Interval (CI) of the between groups GMTs ratio at day 31 (ie, one month after the second vaccination) does not exceed the range 0.5 (lower limit) - 2.0 (higher limit).

Secondary: 3) Percentage of Subjects with hSBA ≥1:5 against each of N. meningitidis serogroup B test strains.

End point title	3) Percentage of Subjects with hSBA ≥1:5 against each of N. meningitidis serogroup B test strains.

End point description:

The immune response of two different lots of rMenB+OMV NZ against each of N. meningitidis serogroup B test strains is evaluated in terms of percentages of subjects with hSBA ≥1:5.

End point type	Secondary

End point timeframe:

Day 61

End point values	4CMenB_Rosia	4CMenB_Siena		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	147[9]	152[10]		
Units: Percentages of Subjects				
number (confidence interval 95%)				
H44/76 strain	99 (96 to 100)	99 (96 to 100)		
NZ98/254 strain	70 (62 to 77)	79 (72 to 86)		
5/99 strain	100 (98 to 100)	100 (98 to 100)		

Notes:

[9] - Analysis was done on the Per Protocol Set.

[10] - Analysis was done on the Per Protocol Set

Statistical analyses

No statistical analyses for this end point

Secondary: 4) Geometric Mean Ratio (GMR) of GMTs against each of N. meningitidis serogroup B reference strains.

End point title	4) Geometric Mean Ratio (GMR) of GMTs against each of N. meningitidis serogroup B reference strains.

End point description:

The immune response of two different lots of rMenB+OMV NZ against each of N. meningitidis serogroup B test strains is evaluated in terms of GMR between GMTs (1month after 2nd vaccination vs baseline).

End point type	Secondary

End point timeframe:

Day 61

End point values	4CMenB_Rosia	4CMenB_Siena		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	147[11]	152[12]		
Units: Ratio of GMTs				
geometric mean (confidence interval 95%)				
H44/76 strain (N=147, 151)	104 (89 to 121)	107 (92 to 124)		
NZ98/254 strain (N=147, 151)	8.63 (6.99 to 11)	11 (8.99 to 14)		
5/99 strain	156 (133 to 183)	167 (143 to 195)		

Notes:

[11] - Analysis was done on the Per Protocol Set.

[12] - Analysis was done on the Per Protocol Set.

Statistical analyses

No statistical analyses for this end point

Secondary: 5) GMR of ELISA GMCs against antigen 287-953

End point title	5) GMR of ELISA GMCs against antigen 287-953

End point description:

The immune response of two different lots of rMenB+OMV NZ against antigen 287-953 is evaluated in terms of GMRs between ELISA GMCs (day 61 vs baseline).

End point type	Secondary

End point timeframe:

Day 61

End point values	4CMenB_Rosia	4CMenB_Siena		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	145[13]	152[14]		
Units: Ratio of GMTs				
geometric mean (confidence interval 95%)	122 (103 to 143)	153 (131 to 179)		

Notes:

[13] - Analysis was done on the Per Protocol Set.

[14] - Analysis was done on the Per Protocol Set.

Statistical analyses

No statistical analyses for this end point

Secondary: 6) hSBA GMT against 3 N. meningitidis serogroup B reference strains at

day 45.

End point title	6) hSBA GMT against 3 N. meningitidis serogroup B reference strains at day 45.

End point description:

The immunogenicity of two different lots of rMenB+OMV NZ is evaluated in terms of hSBA GMT against 3 N. Meningitidis serogroup B reference strains at two weeks after last vaccination.

End point type	Secondary

End point timeframe:

Day 45

End point values	4CMenB_Rosia	4CMenB_Siena		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76[15]	71[16]		
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76 strain (N=76,70)	187 (152 to 229)	171 (139 to 210)		
NZ98/254 strain	14 (10 to 18)	20 (15 to 27)		
5/99 strain	254 (206 to 314)	339 (273 to 420)		

Notes:

[15] - Analysis was done on the PPS, immunogenicity subset.

[16] - Analysis was done on the PPS, immunogenicity subset.

Statistical analyses

No statistical analyses for this end point

Secondary: 7) GMRs of GMT against 3 N. meningitidis serogroup B reference strains at day 45.

End point title	7) GMRs of GMT against 3 N. meningitidis serogroup B reference strains at day 45.

End point description:

The immunogenicity of two different lots of rMenB+OMV NZ is evaluated in terms of GMRs of GMT against 3 N. meningitidis serogroup B reference strains at two weeks after last vaccination.

End point type	Secondary

End point timeframe:

Day 45

End point values	4CMenB_Rosia	4CMenB_Siena		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76[17]	71[18]		
Units: Ratios of GMTs				
geometric mean (confidence interval 95%)				
H44/76 strain (N=76, 70)	174 (138 to 219)	157 (124 to 199)		

NZ98/254 strain	13 (9.87 to 17)	20 (15 to 26)		
5/99 strain	214 (161 to 284)	243 (183 to 325)		

Notes:

[17] - Analysis was done on the PPS, immunogenicity subset.

[18] - Analysis was done on the PPS, immunogenicity subset.

Statistical analyses

No statistical analyses for this end point

Secondary: 8) Percentage of Subjects with hSBA ≥1:5 against each of N. meningitidis serogroup B reference strains at day 45.

End point title	8) Percentage of Subjects with hSBA ≥1:5 against each of N. meningitidis serogroup B reference strains at day 45.

End point description:

The immune response of two different lots of rMenB+OMV NZ against each of N. Meningitidis serogroup B reference strains is evaluated in terms of percentages of subjects with hSBA ≥1:5 two weeks after the last vaccination.

End point type	Secondary

End point timeframe:

Day 45

End point values	4CMenB_Rosia	4CMenB_Siena		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	76[19]	71[20]		
Units: Percentage of Subjects				
number (confidence interval 95%)				
H44/76 strain	100 (95 to 100)	100 (95 to 100)		
NZ98/254 strain	84 (74 to 92)	96 (88 to 99)		
5/99 strain	100 (95 to 100)	100 (95 to 100)		

Notes:

[19] - Analysis was done on the PPS, immunogenicity subset.

[20] - Analysis was done on the PPS, immunogenicity subset.

Statistical analyses

No statistical analyses for this end point

Secondary: 9) ELISA GMCs against vaccine antigen 287-953 at day 45.

End point title	9) ELISA GMCs against vaccine antigen 287-953 at day 45.

End point description:

The immune response of two different lots of rMenB+OMV NZ is evaluated in terms of ELISA GMCs against vaccine antigen 287-953.

End point type	Secondary

End point timeframe:

Day 45

End point values	4CMenB_Rosia	4CMenB_Siena		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74[21]	71[22]		
Units: IU/mL				
geometric mean (confidence interval 95%)	3782 (3011 to 4750)	4824 (3839 to 6061)		

Notes:

[21] - Analysis was done on the PPS, immunogenicity subset.

[22] - Analysis was done on the PPS, immunogenicity subset.

Statistical analyses

No statistical analyses for this end point

Secondary: 10) GMR of ELISA GMCs against antigen 287-953 at day 45.

End point title	10) GMR of ELISA GMCs against antigen 287-953 at day 45.

End point description:

The immune response of two different lots of rMenB+OMV NZ against antigen 287-953 is evaluated in terms of GMRs between ELISA GMCs (day45 vs baseline).

End point type	Secondary

End point timeframe:

Day 45

End point values	4CMenB_Rosia	4CMenB_Siena		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	74[23]	71[24]		
Units: Ratio of GMTs				
geometric mean (confidence interval 95%)	166 (130 to 213)	217 (169 to 279)		

Notes:

[23] - Analysis was done on the PPS, immunogenicity subset.

[24] - Analysis was done on the PPS, immunogenicity subset.

Statistical analyses

No statistical analyses for this end point

Secondary: 11) Number of subjects reporting solicited local and systemic Adverse Events (AEs)

End point title	11) Number of subjects reporting solicited local and systemic Adverse Events (AEs)

End point description:

Number of subjects reporting solicited local and systemic Adverse Events and other indicators of reactogenicity after any vaccination.

End point type	Secondary

End point timeframe:

From day 1 to day 7 after any vaccination.

End point values	4CMenB_Rosia	4CMenB_Siena		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	169[25]	173[26]		
Units: Number of subjects				
Any local	163	170		
Induration	65	74		
Pain	162	170		
Erythema	110	111		
Swelling	80	74		
Any systemic	136	150		
Nausea	49	56		
Fatigue	75	85		
Myalgia	99	118		
Arthralgia	28	44		
Headache	75	89		
Fever (>= 38C)	8	5		
Rash	11	16		
Any other	87	96		
Use of Analgesics	82	92		

Notes:

[25] - Analysis was done on the Safety set.

[26] - Analysis was done on the Safety set.

Statistical analyses

No statistical analyses for this end point

Secondary: 12) Number of subjects reporting Unsolicited AEs

End point title	12) Number of subjects reporting Unsolicited AEs

End point description:

Number of subjects reporting any Unsolicited AEs after any vaccination.

End point type	Secondary

End point timeframe:

From day 1 to day 7 after any vaccination .

End point values	4CMenB_Rosia	4CMenB_Siena		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	169[27]	173[28]		
Units: Number of subjects	56	55		

Notes:

[27] - Analysis was done on the Safety set.

[28] - Analysis was done on the Safety set.

Statistical analyses

No statistical analyses for this end point

Secondary: 13) Number of subjects reporting SAEs and AE leading to withdrawal

End point title	13) Number of subjects reporting SAEs and AE leading to withdrawal

End point description:

Number of subjects any Serious AEs (SAEs), medically attended AEs and AEs that result in a subject's withdrawal from the study after any vaccination.

End point type	Secondary

End point timeframe:

Throughout the entire study period.

End point values	4CMenB_Rosia	4CMenB_Siena		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	169[29]	173[30]		
Units: Number of subjects				
SAEs	0	0		
AEs leading to withdrawal	0	1		

Notes:

[29] - Analysis was done on the Safety set.

[30] - Analysis was done on the Safety set.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SAEs were collected from day 1 through study termination, other AEs were collected from day 1 to 7 after vaccination.

Adverse event reporting additional description:

Solicited adverse events were collected through systematic assessment, unsolicited were collected through non-systematic assessment. Analysis was done on the Safety set.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups

Reporting group title	4CMenB_Siena

Reporting group description:

Subjects received two doses of rMenB+OMV NZ vaccinations from lot 2 manufactured at Siena facility.

Reporting group title	4CMenB_Rosia

Reporting group description:

Subjects received two doses of rMenB+OMV NZ vaccine from lot 1 manufactured at Rosia facility.

Serious adverse events	4CMenB_Siena	4CMenB_Rosia	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 173 (0.00%)	0 / 169 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	4CMenB_Siena	4CMenB_Rosia	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	171 / 173 (98.84%)	165 / 169 (97.63%)	
Investigations			
Injection Site Swelling			
subjects affected / exposed	74 / 173 (42.77%)	80 / 169 (47.34%)	
occurrences (all)	107	115	
Nervous system disorders			
Headache			
subjects affected / exposed	89 / 173 (51.45%)	75 / 169 (44.38%)	
occurrences (all)	159	124	

General disorders and administration site conditions			
Fatigue			
alternative assessment type: Systematic			
subjects affected / exposed	85 / 173 (49.13%)	75 / 169 (44.38%)	
occurrences (all)	138	129	
Injection Site Erythema			
alternative assessment type: Systematic			
subjects affected / exposed	111 / 173 (64.16%)	111 / 169 (65.68%)	
occurrences (all)	177	175	
Injection Site Pain			
alternative assessment type: Systematic			
subjects affected / exposed	170 / 173 (98.27%)	162 / 169 (95.86%)	
occurrences (all)	349	337	
Injection Site Induration			
subjects affected / exposed	75 / 173 (43.35%)	65 / 169 (38.46%)	
occurrences (all)	107	96	
Gastrointestinal disorders			
Nausea			
alternative assessment type: Systematic			
subjects affected / exposed	56 / 173 (32.37%)	49 / 169 (28.99%)	
occurrences (all)	77	68	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	16 / 173 (9.25%)	11 / 169 (6.51%)	
occurrences (all)	18	13	
Musculoskeletal and connective tissue disorders			
Myalgia			
alternative assessment type: Systematic			
subjects affected / exposed	118 / 173 (68.21%)	99 / 169 (58.58%)	
occurrences (all)	189	169	
Arthralgia			
subjects affected / exposed	45 / 173 (26.01%)	28 / 169 (16.57%)	
occurrences (all)	66	38	

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