Clinical trial results:
A Phase 3B, Open Label, Multi-Center Study to Evaluate the Safety, Tolerability and Immunogenicity of Novartis Meningococcal B Recombinant Vaccine When Administered Alone to Healthy Infants According to Different Immunization Schedules and to Healthy Children Aged 2 to 10 Years

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

EudraCT number	2010-021528-81
Trial protocol	ES HU
Global end of trial date	01 July 2015

Results information

Result version number	v1 (current)
This version publication date	15 April 2016
First version publication date	15 April 2016

Trial information

Trial identification

Sponsor protocol code	V72_28

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01339923
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Vaccines and Diagnostics
Sponsor organisation address	Via Fiorentina 1, Siena, Italy, 53100
Public contact	Study Start-up Associate, ICON Clinical Research Ltd, +36 28471689, zsuzsanna.tribel@iconplc.com
Scientific contact	Study Start-up Associate, ICON Clinical Research Ltd, +36 28471689, zsuzsanna.tribel@iconplc.com
Sponsor organisation name	Novartis Vaccines and Diagnostics
Sponsor organisation address	Via Fiorentina 1, Siena, Italy, 53100
Public contact	Posting Director, Novartis Vaccines and Diagnostics, RegistryContactVaccinesUS@novartis.com
Scientific contact	Posting Director, Novartis Vaccines and Diagnostics, RegistryContactVaccinesUS@novartis.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan	EMEA-000139-PIP01-07

number(s)	
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	01 July 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 December 2014
Global end of trial reached?	Yes
Global end of trial date	01 July 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate a sufficient immune response following rMenB+OMV NZ vaccination, when given as a two dose primary series to healthy infants at 3 1/2 and 5 months of age or at 6 and 8 months of age, as measured by the percentage of subjects with serum bactericidal activity (SBA) titers of at least 4, at 1 month after the second rMenB+OMV NZ dose, directed against MenB indicator strains H44/76, 5/99 and NZ98/254.

Protection of trial subjects:

This clinical study was designed, implemented and reported in accordance with the ICH Harmonized Tripartite Guidelines for Good Clinical Practice, 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	06 April 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	Brazil: 417
Country: Number of subjects enrolled	Peru: 59
Country: Number of subjects enrolled	Spain: 653
Country: Number of subjects enrolled	Hungary: 280
Worldwide total number of subjects	1409
EEA total number of subjects	933

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)	1005
Children (2-11 years)	404
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:

The study was conducted in a total of a total of 26 sites; 4 sites in Brazil, 3 sites in Peru, 10 sites in Hungary, 9 sites in Spain.

Pre-assignment

Screening details:

All enrolled subjects were included in the study.

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	B_2h3h5_11

Arm description:

Subjects approximately 2.5 months of age received 3 dose primary vaccination of rMenB+OMV NZ at 2.5, 3.5, 5 months of age, followed by a booster dose at 11 months of age.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (group B) multicomponent recombinant adsorbed vaccine
Investigational medicinal product code	
Other name	rMenB+OMV NZ
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

rMenB+OMV NZ Vaccine: Administration was done intramuscularly (IM), 3 doses + booster, of 0.5 mL each.

Arm title	B_3h5_11

Arm description:

Subjects approximately 3.5 months of age received 2 dose primary vaccination of rMenB+OMV NZ at 3.5 and 5 months of age, followed by a booster dose at 11 months of age.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (group B) multicomponent recombinant adsorbed vaccine
Investigational medicinal product code	
Other name	rMenB+OMV NZ
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

rMenB+OMV NZ Vaccine: Administration was done IM, 2 doses + booster, of 0.5 mL each.

Arm title	B_68_11

Arm description:

Subjects approximately 6 months of age received 2 dose primary vaccination of rMenB+OMV NZ at 6 and 8 months of age, followed by a booster dose at 11 months of age.

Arm type	Experimental

Investigational medicinal product name	Meningococcal (group B) multicomponent recombinant adsorbed vaccine
Investigational medicinal product code	
Other name	rMenB+OMV NZ
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

rMenB+OMV NZ Vaccine: Administration was done IM, 2 doses + booster, of 0.5 mL each.

Arm title	B_02_2_5

Arm description:

Subjects 2-5 years of age received 2 catch-up doses of rMenB+OMV NZ, each at 0 and 2 months. Blood draw at 0 and 3 months since study start.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (group B) multicomponent recombinant adsorbed vaccine
Investigational medicinal product code	
Other name	rMenB+OMV NZ
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

rMenB+OMV NZ vaccine: Administration was done IM, 2 doses + booster, of 0.5 mL each.

Arm title	BC_35_12

Arm description:

Subjects 3 months of age received rMenB+OMV NZ + MenC-CRM and Synflorix concomitantly at 3, 5 and 12 months of age and an additional dose of Synflorix alone dose at 7 months of age.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (group B) multicomponent recombinant adsorbed vaccine Meningococcal (group C) oligosaccharide diptheria CRM-197 conjugate vaccine Synflorix
Investigational medicinal product code	
Other name	rMenB+OMV NZ MenC-CRM Synflorix
Pharmaceutical forms	Powder and solvent for suspension for injection, Suspension for injection, Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

rMenB+OMV NZ vaccine: Administration was done IM, 2 doses + booster, of 0.5 mL each.
MenC-CRM vaccine: Administration was done IM, 2 doses booster, of 0.5 mL each.
Synflorix: Administration was done IM, 3 doses + booster.

Arm title	C_35_12

Arm description:

Subjects 3 months of age received MenCCRM and Synflorix concomitantly at 3, 5 and 12 months of age and an additional dose of Synflorix alone at 7 months of age and rMenB+OMV NZ alone at 13 and 15 months of age.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (group B) multicomponent recombinant adsorbed vaccine Meningococcal (group C) oligosaccharide diphtheria CRM-197 conjugate vaccine Synflorix
Investigational medicinal product code	
Other name	rMenB+OMV NZ MenC-CRM Synflorix
Pharmaceutical forms	Powder and solvent for suspension for injection, Suspension for injection, Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

rMenB+OMV NZ vaccine: Administration was done IM, 2 doses + booster, of 0.5 mL each.
MenC-CRM vaccine: Administration was done IM, 2 doses + booster, of 0.5 mL each.
Synflorix: Administration was done IM, 3 doses + booster.

Arm title	B_02_6_10

Arm description:

Subjects 6-10 years of age received 2 catch-up doses of rMenB+OMV NZ, each at 0 and 2 months. Blood draw at 0 and 3 months since study start.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (group B) multicomponent recombinant adsorbed vaccine
Investigational medicinal product code	
Other name	rMenB+OMV NZ
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

rMenB+OMV NZ vaccine: Administration was done IM, 2 doses + booster, of 0.5 mL each.

Number of subjects in period 1	B_2h3h5_11	B_3h5_11	B_68_11
Started	253	250	251
Completed	239	234	243
Not completed	14	16	8
Consent withdrawn by subject	7	11	6
Adverse event, non-fatal	1	1	1
Inappropriate enrollment	1	-	-
Unable to classify	1	-	1
Lost to follow-up	4	4	-
Protocol deviation	-	-	-

Number of subjects in period 1	B_02_2_5	BC_35_12	C_35_12
Started	104	126	125
Completed	100	117	111
Not completed	4	9	14
Consent withdrawn by subject	1	3	2
Adverse event, non-fatal	-	-	1
Inappropriate enrollment	-	1	-
Unable to classify	-	1	5
Lost to follow-up	3	1	5
Protocol deviation	-	3	1

Number of subjects in period 1	B_02_6_10
Started	300
Completed	295
Not completed	5
Consent withdrawn by subject	4
Adverse event, non-fatal	-

Inappropriate enrollment	-
Unable to classify	-
Lost to follow-up	1
Protocol deviation	-

Baseline characteristics

Reporting groups	
Reporting group title	B_2h3h5_11
Reporting group description:	
Subjects approximately 2.5 months of age received 3 dose primary vaccination of rMenB+OMV NZ at 2.5, 3.5, 5 months of age, followed by a booster dose at 11 months of age.	
Reporting group title	B_3h5_11
Reporting group description:	
Subjects approximately 3.5 months of age received 2 dose primary vaccination of rMenB+OMV NZ at 3.5 and 5 months of age, followed by a booster dose at 11 months of age.	
Reporting group title	B_68_11
Reporting group description:	
Subjects approximately 6 months of age received 2 dose primary vaccination of rMenB+OMV NZ at 6 and 8 months of age, followed by a booster dose at 11 months of age.	
Reporting group title	B_02_2_5
Reporting group description:	
Subjects 2-5 years of age received 2 catch-up doses of rMenB+OMV NZ, each at 0 and 2 months. Blood draw at 0 and 3 months since study start.	
Reporting group title	BC_35_12
Reporting group description:	
Subjects 3 months of age received rMenB+OMV NZ + MenC-CRM and Synflorix concomitantly at 3, 5 and 12 months of age and an additional dose of Synflorix alone dose at 7 months of age.	
Reporting group title	C_35_12
Reporting group description:	
Subjects 3 months of age received MenCCRM and Synflorix concomitantly at 3, 5 and 12 months of age and an additional dose of Synflorix alone at 7 months of age and rMenB+OMV NZ alone at 13 and 15 months of age.	
Reporting group title	B_02_6_10
Reporting group description:	
Subjects 6-10 years of age received 2 catch-up doses of rMenB+OMV NZ, each at 0 and 2 months. Blood draw at 0 and 3 months since study start.	

Reporting group values	B_2h3h5_11	B_3h5_11	B_68_11
Number of subjects	253	250	251
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous Units: months			
arithmetic mean	2	3	6
standard deviation	± 0.1	± 0.1	± 0

Gender categorical Units: Subjects			
Female	117	124	127
Male	136	126	124

Reporting group values	B_02_2_5	BC_35_12	C_35_12
Number of subjects	104	126	125
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous Units: months			
arithmetic mean	3.958	3	3
standard deviation	± 1.117	± 0.2	± 0.1
Gender categorical Units: Subjects			
Female	49	74	59
Male	55	52	66

Reporting group values	B_02_6_10	Total	
Number of subjects	300	1409	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		0	
Newborns (0-27 days)		0	
Infants and toddlers (28 days-23 months)		0	
Children (2-11 years)		0	
Adolescents (12-17 years)		0	
Adults (18-64 years)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: months			
arithmetic mean	8.074		
standard deviation	± 1.404	-	
Gender categorical Units: Subjects			
Female	149	699	
Male	151	710	

End points

End points reporting groups

Reporting group title	B_2h3h5_11
Reporting group description:	
Subjects approximately 2.5 months of age received 3 dose primary vaccination of rMenB+OMV NZ at 2.5, 3.5, 5 months of age, followed by a booster dose at 11 months of age.	
Reporting group title	B_3h5_11
Reporting group description:	
Subjects approximately 3.5 months of age received 2 dose primary vaccination of rMenB+OMV NZ at 3.5 and 5 months of age, followed by a booster dose at 11 months of age.	
Reporting group title	B_68_11
Reporting group description:	
Subjects approximately 6 months of age received 2 dose primary vaccination of rMenB+OMV NZ at 6 and 8 months of age, followed by a booster dose at 11 months of age.	
Reporting group title	B_02_2_5
Reporting group description:	
Subjects 2-5 years of age received 2 catch-up doses of rMenB+OMV NZ, each at 0 and 2 months. Blood draw at 0 and 3 months since study start.	
Reporting group title	BC_35_12
Reporting group description:	
Subjects 3 months of age received rMenB+OMV NZ + MenC-CRM and Synflorix concomitantly at 3, 5 and 12 months of age and an additional dose of Synflorix alone dose at 7 months of age.	
Reporting group title	C_35_12
Reporting group description:	
Subjects 3 months of age received MenCCRM and Synflorix concomitantly at 3, 5 and 12 months of age and an additional dose of Synflorix alone at 7 months of age and rMenB+OMV NZ alone at 13 and 15 months of age.	
Reporting group title	B_02_6_10
Reporting group description:	
Subjects 6-10 years of age received 2 catch-up doses of rMenB+OMV NZ, each at 0 and 2 months. Blood draw at 0 and 3 months since study start.	
Subject analysis set title	All Enrolled Set
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
All subjects enrolled in the study, ie., all screened subjects who provided informed consent and provided demographic and/or baseline assessments, regardless of the subjects' randomization and treatment status in the trial.	
Subject analysis set title	Full Analysis set (FAS; Immunogenicity; Primary series)
Subject analysis set type	Full analysis
Subject analysis set description:	
All subjects in enrolled population who received at least one rMenB+OMV NZ dose or MenC-CRM (group C3512) and provided an evaluable serum sample at relevant time points (visit 4 for group B_2h3h5_11 and visit 3 for groups B_3h5_11, B_68_11, B_02, BC_35_12 and C_35_12).	
Subject analysis set title	Full Analysis set (FAS; Immunogenicity; Post first dose respon
Subject analysis set type	Full analysis
Subject analysis set description:	
All subjects enrolled in Groups B_2h3h5_11b, B_3h5_11b and B_68_11b who received at least one rMenB+OMV NZ dose and provided an evaluable serum sample at 1, 1.5 and 2 months, respectively, after the first vaccination (visit 2).	
Subject analysis set title	Full Analysis set (Immunogenicity; persistence)
Subject analysis set type	Full analysis
Subject analysis set description:	
All subjects in enrolled population who received at least one rMenB+OMV NZ dose or MenC-CRM (group	

C_35_12) and provided an evaluable
serum sample at relevant time points (visit 5 for groups B_2h_3h511, BC_35_12, C_35_12 and visit 4 for groups B_3h5_11, B_68_11).

Subject analysis set title	Full Analysis set (Immunogenicity; Booster)
Subject analysis set type	Full analysis

Subject analysis set description:

All subjects in enrolled population who received at least one rMenB+OMV NZ dose or MenC-CRM (group C_35_12) and provided an evaluable
serum sample at relevant time points (visit 6 for groups B_2h_3h5_11, BC_35_12, C_35_12 and visit 5 for groups B_3h5_11, B_68_11).

Subject analysis set title	Per protocol set (PPS; Immunogenicity; Primary series)
Subject analysis set type	Per protocol

Subject analysis set description:

All subjects in FAS population, who correctly received all doses of vaccine in primary series, provided evaluable serum sample at relevant time points (visit 4 for group B_2h3h5_11 and visit 3 for groups B_3h5_11, B_68_11, B_02, BC_35_12 and C_35_12) and have no major protocol deviations.

Subject analysis set title	Per protocol set (PPS; Immunogenicity; Post first dose respons
Subject analysis set type	Per protocol

Subject analysis set description:

All subjects in FAS population, who correctly received all doses of vaccine in primary series, provided evaluable serum sample at relevant time
points (visit 5 for groups B_2h3h5_11, BC_35_12, C_35_12 and visit 4 for groups B_3h5_11, B_68_11) and have no major protocol deviations.

Subject analysis set title	Per protocol set (Immunogenicity; Booster)
Subject analysis set type	Per protocol

Subject analysis set description:

All subjects in FAS population, who correctly received all doses of vaccine in primary series and booster dose, provided evaluable serum sample at relevant time points (visit 6 for groups B_2h3h5_11, BC_35_12, C_35_12 and visit 5 for groups B_3h5_11, B_68_11) and have no major protocol deviations.

Subject analysis set title	Overall safety set
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects in the enrolled set, who received a study vaccination and provided solicited or unsolicited adverse event data.

Subject analysis set title	Solicited safety set
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects in the enrolled set, who received a study vaccination and provided any solicited adverse event data or indicators of solicited adverse events

Subject analysis set title	Unsolicited safety set
Subject analysis set type	Safety analysis

Subject analysis set description:

All subjects in the enrolled set, who received a study vaccination and provided unsolicited adverse event data.

Subject analysis set title	B_2h3h5_11b
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects, approximately 2.5 months of age received 3 dose primary vaccination of rMenB+OMV NZ at 2.5, 3.5, 5 months of age, followed by a booster dose at 11 months of age. Blood draw at 3.5, 6, 11 and 12 months of age.

Subject analysis set title	B_3h5_11b
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects, approximately 3.5 months of age received 2 dose primary vaccination of rMenB+OMV NZ at 3.5 and 5 months of age, followed by a
booster dose at 11 months of age. Blood draw at 5, 11 and 12 months of age.

Subject analysis set title	B_68_11b

Subject analysis set type	Full analysis

Subject analysis set description:

Subjects, approximately 6 months of age received 2 dose primary vaccination of rMenB+OMV NZ at 3.5 and 5 months of age, followed by a booster dose at 11 months of age. Blood draw at 8, 9, 11 and 12 months of age.

Subject analysis set title	B_02_2_5
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects, 2-5 years of age received 2 catch-up doses of rMenB+OMV NZ, each at 0 and 2 months. Blood draw at 0 and 3 months since study start.

Subject analysis set title	B_02_6_10
Subject analysis set type	Safety analysis

Subject analysis set description:

Subjects, 6-10 years of age received 2 catch-up doses of rMenB+OMV NZ, each at 0 and 2 months. Blood draw at 0 and 3 months since study start.

Subject analysis set title	B_02
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects, 2-10 years of age received 2 catch-up doses of rMenB+OMV NZ, each at 0 and 2 months. Blood draw at 0 and 3 months since study start.
rMenB + OMV NZ vaccine: 2 doses 2 months apart

Primary: Percentages of Subjects with Serum Bactericidal Activity Using Human Serum (hSBA) Titers ≥ 4 or hSBA Titers ≥ 5 (Strain M10713) Following a 2-dose Primary Series of rMenB+OMV Vaccination

End point title	Percentages of Subjects with Serum Bactericidal Activity Using Human Serum (hSBA) Titers ≥ 4 or hSBA Titers ≥ 5 (Strain M10713) Following a 2-dose Primary Series of rMenB+OMV Vaccination[1][2]

End point description:

Immunogenicity was assessed in terms of percentages of subjects with hSBA titers ≥ 4 against N meningitidis serogroup B strains H44/76, 5/99, NZ98/254 and hSBA titers ≥ 5 against strain M10713 following 2-dose primary series of vaccination with rMenB+OMV NZ at 3.5 and 5 months of age or at 6 and 8 months of age. Analysis was done on Full analysis set (FAS)-Primary series.

End point type	Primary

End point timeframe:

1 month after second vaccination

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 null hypothesis associated with this immunogenicity objective.

[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 null hypothesis associated with this immunogenicity objective.

End point values	B_3h5_11	B_68_11		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	230	238		
Units: Percentages of subjects				
number (confidence interval 97.5%)				
H44/76 (hSBA≥ 4; N=228, 234)	100 (97 to 100)	100 (97 to 100)		
5/99 (hSBA≥ 4)	100 (97 to 100)	100 (98 to 100)		
NZ98/254 (hSBA≥ 4; N=230, 233)	98 (95 to 99)	99 (97 to 100)		
M10713 (hSBA≥ 5; N=181, 192)	44 (35 to 52)	73 (65 to 80)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of Subjects with hSBA Titers ≥ 4, hSBA Titers ≥ 5 (Strain M10713) and hSBA ≥ 8 Following a 3-dose Primary Series of rMenB+OMV Vaccination

End point title	Percentages of Subjects with hSBA Titers ≥ 4, hSBA Titers ≥ 5 (Strain M10713) and hSBA ≥ 8 Following a 3-dose Primary Series of rMenB+OMV Vaccination[3]

End point description:

Immunogenicity was assessed in terms of percentages of subjects with hSBA titers ≥ 4 against N meningitidis serogroup B strains H44/76, 5/99, NZ98/254; hSBA titers ≥ 5 against strain M10713 and hSBA titers ≥ 8 against strains H44/76, 5/99, NZ98/254, M10713, following 3-dose primary series of vaccination with rMenB+OMV NZ at 2.5, 3.5 and 5 months of age. Analysis was done on FAS-primary series.

End point type	Secondary

End point timeframe:

1 month after third vaccination

Notes:

[3] - 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 null hypothesis associated with this immunogenicity objective.

End point values	B_2h3h5_11			
Subject group type	Reporting group			
Number of subjects analysed	238			
Units: Percentage				
number (confidence interval 95%)				
H44/76 (hSBA≥ 4; 1 month after 3rd vacc; N=237)	100 (98 to 100)			
5/99 (hSBA≥ 4; 1 month after 3rd vacc)	100 (98 to 100)			
NZ98/254 (hSBA≥ 4; 1 month after 3rd vacc)	99 (96 to 100)			
M10713 (hSBA≥ 5; 1 month after 3rd vacc; N=197)	55 (48 to 62)			
H44/76 (hSBA≥ 8; 1 month after 3rd vacc; N=237)	98 (96 to 100)			
5/99 (hSBA≥ 8; 1 month after 3rd vacc)	100 (98 to 100)			
NZ98/254 (hSBA≥ 8; 1 month after 3rd vacc)	89 (85 to 93)			
M10713 (hSBA≥ 8; 1 month after 3rd vacc; N=197)	47 (40 to 54)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of Subjects with hSBA Titers ≥ 4 or hSBA Titers ≥ 5 (Strain M10713) and hSBA ≥ 8 Following a 2-dose Catch-up Series of rMenB+OMV Vaccination

End point title	Percentages of Subjects with hSBA Titers ≥ 4 or hSBA Titers ≥ 5 (Strain M10713) and hSBA ≥ 8 Following a 2-dose Catch-up Series of rMenB+OMV Vaccination

End point description:

Immunogenicity was assessed in terms of percentages of subjects with hSBA titers ≥ 4 against N meningitidis serogroup B strains H44/76, 5/99, NZ98/254; hSBA titers ≥ 5 against strain M10713 and hSBA titers ≥ 8 against strains H44/76, 5/99, NZ98/254, M10713; following 2-dose catch-up series of vaccination with rMenB+OMV NZ in healthy children aged 2-10 years (0, 2 month schedule). Analysis was done on FAS-primary series.

End point type	Secondary

End point timeframe:

1 month after second vaccination

End point values	B_02			
Subject group type	Subject analysis set			
Number of subjects analysed	390			
Units: Percentage				
number (confidence interval 95%)				
H44/76 (hSBA≥ 4; 1 month after 2nd vacc; N=386)	99 (97 to 100)			
5/99 (hSBA≥ 4; 1 month after 2nd vacc)	99 (98 to 100)			
NZ98/254 (hSBA≥ 4; 1 month after 2nd vacc; N=389)	99 (97 to 100)			
M10713 (hSBA≥ 5; 1 month after 2nd vacc; N=370)	94 (91 to 96)			
H44/76 (hSBA≥ 8; 1 month after 2nd vacc; N=386)	98 (96 to 99)			
5/99 (hSBA≥ 8; 1 month after 2nd vacc)	99 (98 to 100)			
NZ98/254 (hSBA≥ 8; 1 month after 2nd vacc; N=389)	95 (92 to 97)			
M10713 (hSBA≥ 8; 1 month after 2nd vacc; N=370)	92 (89 to 94)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of Subjects Achieving Four-fold Rise Over Baseline hSBA Titers Following a 2-dose Catch-up Series of rMenB+OMV Vaccination

End point title	Percentages of Subjects Achieving Four-fold Rise Over Baseline hSBA Titers Following a 2-dose Catch-up Series of rMenB+OMV Vaccination

End point description:

Immunogenicity was assessed in terms of percentages of subjects achieving 4-fold increase in hSBA

titers as compared to baseline against N meningitidis serogroup B strains H44/76, 5/99, NZ98/254, M10713; following 2-dose catch-up series of vaccination with rMenB+OMV NZ in healthy children aged 2-10 years (0, 2 month schedule). Analysis was done on FAS- primary series.

End point type	Secondary

End point timeframe:

1 month after second vaccination

End point values	B_02			
Subject group type	Subject analysis set			
Number of subjects analysed	388			
Units: Percentage				
number (confidence interval 95%)				
H44/76 (1 month after 2nd vacc; N=385)	96 (93 to 97)			
5/99 (1 month after 2nd vacc)	99 (97 to 100)			
NZ98/254 (1 month after 2nd vacc; N=387)	93 (89 to 95)			
M10713 (1 month after 2nd vacc; N=352)	46 (41 to 51)			

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean hSBA Titers (GMTs) Following 2 or 3 Dose Primary Series of Vaccination with rMenB+OMV

End point title	Geometric Mean hSBA Titers (GMTs) Following 2 or 3 Dose Primary Series of Vaccination with rMenB+OMV[4]

End point description:

Immunogenicity was assessed in terms of Geometric mean hSBA titers (GMTs) against N meningitidis serogroup B indicator strains following 2 or 3 dose primary series of vaccination rMenB+OMV NZ (1 month after 3rd infant vaccination in B_2h3h5_11 and 1 month after 2nd infant vaccination in B_3h5_11, B_68_11 and B_02). Analysis was done on FAS-primary series.

End point type	Secondary

End point timeframe:

1 month after primary series vaccination

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 null hypothesis associated with this immunogenicity objective.

End point values	B_2h3h5_11	B_3h5_11	B_68_11	B_02
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	238	230	238	390
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76 (1 m after primary vacc; N=237,228,234,386)	109 (92 to 130)	132 (110 to 158)	240 (201 to 287)	121 (109 to 135)

5/99 (1 m after primary vacc)	795 (665 to 950)	605 (502 to 729)	1157 (964 to 1390)	489 (442 to 541)
NZ98/254 1 m after primary vacc; N=238,230,233,389	34 (28 to 42)	39 (31 to 48)	65 (52 to 80)	42 (38 to 47)
M10713 (1 m after primary vacc; N=197,181,192,370)	4.86 (3.62 to 6.54)	3.39 (2.48 to 4.64)	9.96 (7.33 to 14)	35 (31 to 39)

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean hSBA Titers (GMTs) After First Infant Vaccination with rMenB+OMV

End point title	Geometric Mean hSBA Titers (GMTs) After First Infant Vaccination with rMenB+OMV

End point description:

Immunogenicity was assessed in terms of Geometric mean hSBA titers (GMTs) against N meningitidis serogroup B indicator strains after the first infant vaccination in groups B_2h3h5_11b, B_3h5_11b and B_68_11b (after 1 month for group B_2h3h5_11b, 1.5 months for group B_2h3h5_11b and 2 months for group B_68_11b). Analysis was done on FAS-post first dose.

End point type	Secondary

End point timeframe:

1, 1.5 or 2 months after first infant vaccination

End point values	B_2h3h5_11b	B_3h5_11b	B_68_11b	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	119	115	118	
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76 1 month after 1st vacc; N=117,115,117	4.19 (3.29 to 5.35)	5.7 (4.41 to 7.37)	9.83 (7.59 to 13)	
5/99 1 month after 1st vacc	20 (15 to 27)	30 (22 to 42)	37 (27 to 52)	
NZ98/254 1 month after 1st vacc; N=118,114,117	2.87 (2.32 to 3.54)	2.48 (1.98 to 3.11)	2.84 (2.28 to 3.55)	
M10713 1 month after 1st vacc; N=95,99,95	2.59 (1.86 to 3.6)	1.69 (1.21 to 2.36)	1.62 (1.15 to 2.28)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of Subjects with hSBA Titers ≥ 4 or hSBA Titers ≥ 5 and hSBA ≥ 8 After First Infant Vaccination with rMenB+OMV

End point title	Percentages of Subjects with hSBA Titers ≥ 4 or hSBA Titers ≥ 5 and hSBA ≥ 8 After First Infant Vaccination with rMenB+OMV

End point description:

Immunogenicity was assessed in terms of percentages of subjects with hSBA titers ≥ 4 against N

meningitidis serogroup B strains H44/76, 5/99, NZ98/254, hSBA titers ≥ 5 against strain M10713 and hSBA titers ≥ 8 against strains H44/76, 5/99, NZ98/254, M10713 after the first infant vaccination in groups B_2h3h5_11b, B_3h5_11b and B_68_11b (at 3.5, 5, and 8 months of age respectively). Analysis was done on FAS-post first dose.

End point type	Secondary

End point timeframe:

Post- first dose (1 month for B_2h3h5_11b, 1.5 month for B_3h5_11b and 2 months for B_68_11b after 1st vaccination)

End point values	B_2h3h5_11b	B_3h5_11b	B_68_11b	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	119	115	118	
Units: Percentage				
number (confidence interval 95%)				
H44/76 (hSBA≥ 4; Post 1st vacc; N=117,115,117)	62 (52 to 70)	72 (63 to 80)	82 (74 to 89)	
5/99 (hSBA≥ 4; Post 1st vacc)	91 (84 to 95)	95 (89 to 98)	92 (86 to 96)	
NZ98/254 (hSBA≥ 4; Post 1st vacc; N=118,114,117)	43 (34 to 53)	39 (30 to 48)	41 (32 to 50)	
M10713 (hSBA≥ 5; Post1st vacc; N=95,99,95)	31 (21 to 41)	18 (11 to 27)	17 (10 to 26)	
H44/76 (hSBA≥ 8; Post 1st vacc; N=117,115,117)	25 (17 to 34)	38 (29 to 48)	58 (49 to 67)	
5/99 (hSBA≥ 8; Post1st vacc)	82 (73 to 88)	90 (82 to 94)	86 (79 to 92)	
NZ98/254 (hSBA≥ 8; 1st vacc; N=118,114,117)	13 (7 to 20)	7 (3 to 13)	13 (7 to 20)	
M10713 (hSBA≥ 8; Post1st vacc; N=95,99,95)	21 (13 to 31)	15 (9 to 24)	13 (7 to 21)	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of Subjects with hSBA Titers ≥ 4 or hSBA Titers ≥ 5 and hSBA ≥ 8 Following a Booster Dose of rMenB +OMV Vaccination

End point title	Percentages of Subjects with hSBA Titers ≥ 4 or hSBA Titers ≥ 5 and hSBA ≥ 8 Following a Booster Dose of rMenB +OMV Vaccination[5]

End point description:

Immunogenicity was assessed in terms of percentages of subjects with hSBA titers ≥ 4 against N meningitidis serogroup B strains H44/76, 5/99, NZ98/254; hSBA titers ≥ 5 against strain M10713; hSBA titers ≥ 8 against strains H44/76, 5/99, NZ98/254, M10713; following a booster dose of rMenB+OMV NZ given at 11 months of age (4th dose for B_2h3h5_11 and 3rd dose for B_3h5_11 and B_68_11). Analysis was done on FAS-booster.

End point type	Secondary

End point timeframe:

1 month post-booster dose

Notes:

[5] - 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 null hypothesis associated with this immunogenicity objective.

End point values	B_2h3h5_11	B_3h5_11	B_68_11	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	233	228	239	
Units: Percentage				
number (confidence interval 95%)				
H44/76 (hSBA≥ 4, after booster; N=233,227,238)	100 (98 to 100)	100 (98 to 100)	100 (98 to 100)	
5/99 (hSBA≥ 4, after booster)	100 (98 to 100)	100 (98 to 100)	100 (98 to 100)	
NZ98/254 (hSBA≥ 4, after booster; N=231,226,236)	100 (98 to 100)	99 (96 to 100)	100 (98 to 100)	
M10713 (hSBA≥ 5, after booster; N=203,181,193)	83 (77 to 88)	87 (81 to 91)	83 (77 to 88)	
H44/76 (hSBA≥ 8, after booster; N=233,227,238)	100 (98 to 100)	100 (98 to 100)	100 (98 to 100)	
5/99 (hSBA≥ 8, after booster)	100 (98 to 100)	100 (98 to 100)	100 (98 to 100)	
NZ98/254 (hSBA≥ 8, after booster; N=231,226,236)	95 (91 to 97)	95 (91 to 98)	97 (95 to 99)	
M10713 (hSBA≥ 8, after booster; N=203,181,193)	78 (72 to 84)	83 (77 to 89)	74 (67 to 80)	

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody Persistence in Terms of Percentages of Subjects with hSBA Titers ≥ 4 or hSBA Titers ≥ 5 (M10713) and hSBA ≥ 8 Following 2 or 3-dose Primary Series of Vaccination with rMenB+OMV NZ

End point title	Antibody Persistence in Terms of Percentages of Subjects with hSBA Titers ≥ 4 or hSBA Titers ≥ 5 (M10713) and hSBA ≥ 8 Following 2 or 3-dose Primary Series of Vaccination with rMenB+OMV NZ[6]

End point description:

Persistence of bactericidal antibodies at 11 months of age was assessed in terms of percentages of subjects with hSBA titers ≥ 4 against N meningitidis serogroup B strains H44/76, 5/99, NZ98/254; hSBA titers ≥ 5 against strain M10713; hSBA titers ≥ 8 against strains H44/76, 5/99, NZ98/254, M10713 in subjects who previously received a primary series of 2 or 3-doses of rMenB+OMV NZ vaccine. Analysis was done on FAS-persistence.

End point type	Secondary

End point timeframe:

11 months of age (persistence)

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: There was no statistical null hypothesis associated with this immunogenicity objective.

End point values	B_2h3h5_11	B_3h5_11	B_68_11	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	235	233	238	
Units: Percentage				
number (confidence interval 95%)				
H44/76 (hSBA≥ 4; 11 months of age; N=235,232,237)	87 (82 to 91)	86 (81 to 90)	100 (98 to 100)	

5/99 (hSBA≥ 4; 11 months of age; N=234,230,235)	100 (98 to 100)	93 (89 to 96)	100 (98 to 100)	
NZ98/254 hSBA≥ 4; 11 months of age; N=233,233,238)	54 (47 to 60)	41 (34 to 47)	90 (85 to 93)	
M10713 (hSBA≥ 5; 11 months of age; N=199,177,188)	33 (26 to 40)	23 (17 to 30)	42 (35 to 49)	
H44/76 (hSBA≥ 8; 11 months of age; N=235,232,237)	64 (58 to 70)	60 (53 to 66)	96 (93 to 98)	
5/99 (hSBA≥ 8; 11 months of age; N=234,230,235)	94 (91 to 97)	87 (82 to 91)	99 (97 to 100)	
NZ98/254 hSBA≥ 8; 11 months of age; N=233,233,238)	36 (30 to 43)	12 (8 to 17)	65 (58 to 71)	
M10713 (hSBA≥ 8; 11 months of age; N=199,177,188)	24 (18 to 30)	16 (11 to 22)	36 (29 to 43)	

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody Persistence in Terms of Geometric Mean Titers Following 2 or 3-dose Primary Series of Vaccination with rMenB+OMV NZ

End point title	Antibody Persistence in Terms of Geometric Mean Titers Following 2 or 3-dose Primary Series of Vaccination with rMenB+OMV NZ[7]

End point description:

Persistence of bactericidal antibodies at 11 months of age was assessed in terms of GMTs against N meningitidis serogroup B indicator strains in subjects who previously received a primary series of 2 or 3-doses of rMenB+OMV NZ. Analysis was done on FAS-persistence.

End point type	Secondary

End point timeframe:

11 months of age (persistence)

Notes:

[7] - 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 null hypothesis associated with this immunogenicity objective.

End point values	B_2h3h5_11	B_3h5_11	B_68_11	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	235	233	238	
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76 (Baseline; N=111,113,120)	1.31 (1.09 to 1.57)	1.34 (1.11 to 1.62)	1.58 (1.32 to 1.9)	
H44/76 (11 moa; N=235,232,237)	12 (9.64 to 14)	12 (9.36 to 14)	66 (54 to 81)	
5/99 (Baseline; N=113,112,120)	1.15 (1.02 to 1.3)	1.16 (1.02 to 1.32)	0.97 (0.85 to 1.09)	
5/99 (11 moa; N=234,230,235)	98 (78 to 124)	50 (39 to 63)	285 (225 to 363)	
NZ98/254 (Baseline; N=113,113,122)	1.07 (0.99 to 1.15)	1.04 (0.96 to 1.12)	1 (0.93 to 1.07)	
NZ98/254 (11 moa; N=233,233,238)	4.57 (3.66 to 5.71)	2.68 (2.13 to 3.38)	12 (9.79 to 15)	
M10713 (Baseline; N=84,64,88)	2.36 (1.75 to 3.2)	1.52 (1.07 to 2.17)	1.29 (0.95 to 1.76)	

M10713 (11 moa; N=199,177,188)	2.55 (1.89 to 3.43)	1.98 (1.45 to 2.71)	3.62 (2.66 to 4.94)	

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean ELISA Concentrations Against Vaccine Antigen 287-953 Following 2 or 3-dose Primary Series and Booster Dose of Vaccination with rMenB+OMV NZ

End point title	Geometric Mean ELISA Concentrations Against Vaccine Antigen 287-953 Following 2 or 3-dose Primary Series and Booster Dose of Vaccination with rMenB+OMV NZ[8]

End point description:

Immunogenicity was assessed in terms of Geometric mean ELISA concentrations (GMCs) against N meningitidis serogroup B vaccine antigen 287-953, following 2 or 3 dose primary series and booster dose of rMenB+OMV NZ. Analysis was done on FAS-persistence and FAS-booster.

End point type	Secondary

End point timeframe:

1 month after primary vaccination, pre-booster vaccination (persistence) and 1 month after booster vaccination

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 null hypothesis associated with this immunogenicity objective.

End point values	B_2h3h5_11	B_3h5_11	B_68_11	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	218	225	221	
Units: IU/mL				
geometric mean (confidence interval 95%)				
1 month after primary vaccination (N=212,215,212)	4688 (3884 to 5660)	3152 (2594 to 3831)	4682 (3850 to 5694)	
Pre-booster vaccination (N=213,220,215)	474 (395 to 569)	291 (241 to 351)	1270 (1052 to 1533)	
1 month after booster dose	5900 (5047 to 6898)	6062 (5150 to 7135)	5898 (5016 to 6934)	

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean ELISA Concentrations Against Vaccine Antigen 287-953 After a Two Dose Catch-up rMenB+OMV NZ Immunization Series in Children 2-10 Years of Age

End point title	Geometric Mean ELISA Concentrations Against Vaccine Antigen 287-953 After a Two Dose Catch-up rMenB+OMV NZ Immunization Series in Children 2-10 Years of Age

End point description:

Immunogenicity was assessed in terms of Geometric mean ELISA concentrations (GMCs) against N meningitidis serogroup B vaccine antigen 287-953, after a two dose catch-up immunization series with rMenB+OMV NZ in children 2-10 years of age. Analysis was done on FAS-primary series.

End point type	Secondary

End point timeframe:

1 month after second vaccination

End point values	B_02			
Subject group type	Subject analysis set			
Number of subjects analysed	389			
Units: IU/mL				
geometric mean (confidence interval 95%)	2333 (2124 to 2562)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of Subjects with hSBA Titers ≥ 8 Against Serogroup C Following Concomitant Administration of rMenB +OMV NZ with MenC-CRM or MenC-CRM Alone

End point title	Percentages of Subjects with hSBA Titers ≥ 8 Against Serogroup C Following Concomitant Administration of rMenB +OMV NZ with MenC-CRM or MenC-CRM Alone[9]

End point description:

Non-inferiority of MenC-CRM was determined following co-administration of MenC-CRM and rMenB+OMV NZ or MenC-CRM alone at 3 and 5 months and booster dose at 12 months, as measured by the percentages of subjects achieving hSBA titers ≥ 8 against serogroup C. Analysis was done on PPS-primary series and PPS-booster.

End point type	Secondary

End point timeframe:

Baseline, 1 month after second vaccination and 1 month after booster vaccination

Notes:

[9] - 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 null hypothesis associated with this immunogenicity objective.

End point values	BC_35_12	C_35_12		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	85	72		
Units: Percentage				
number (confidence interval 95%)				
Serogroup C (1 month after 2nd vacc)	99 (94 to 100)	100 (95 to 100)		
Serogroup C (1 month after booster vacc; N=70,47)	100 (95 to 100)	100 (92 to 100)		

Statistical analyses

Statistical analysis title	hSBA≥ 8; 1 month after 2nd vaccination
Statistical analysis description:	
Non-inferiority of MenC-CRM was determined following co-administration of MenC-CRM and rMenB+OMV NZ vs MenC-CRM control group at 1 month after 2nd vaccination for serogroup C.	
Comparison groups	BC_35_12 v C_35_12
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen method
Parameter estimate	Vaccine group difference
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.4
upper limit	3.9

Statistical analysis title	hSBA≥ 8; 1 month after booster vaccination
Statistical analysis description:	
Non-inferiority of MenC-CRM was determined following co-administration of MenC-CRM and rMenB+OMV NZ vs MenC-CRM control group at 1 month after booster vaccination for serogroup C.	
Comparison groups	BC_35_12 v C_35_12
Number of subjects included in analysis	157
Analysis specification	Pre-specified
Analysis type	non-inferiority
Method	Miettinen and Nurminen method
Parameter estimate	Vaccine group difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.2
upper limit	7.6

Secondary: GMTs Following Concomitant Administration of rMenB+OMV NZ with MenC-CRM or MenC-CRM Alone

End point title	GMTs Following Concomitant Administration of rMenB+OMV NZ with MenC-CRM or MenC-CRM Alone[10]

End point description:

Immunogenicity was assessed in terms of GMTs against N meningitidis serogroup C strain following co-administration of MenC-CRM and rMenB+OMV NZ or MenC-CRM alone at 3 and 5 months and booster dose at 12 months. Analysis was done on FAS-primary series and FAS-booster.

End point type	Secondary

End point timeframe:

1 month after second vaccination, 1 month after booster vaccination

Notes:

[10] - 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 null hypothesis associated with this immunogenicity objective.

End point values	BC_35_12	C_35_12		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	102	88		
Units: Titers				
geometric mean (confidence interval 95%)				
1 month after 2nd vacc	568 (461 to 701)	905 (718 to 1141)		
Pre-booster vacc (N=92,75)	36 (28 to 47)	56 (41 to 77)		
1 month after booster vacc (N=99,92)	1201 (991 to 1456)	1724 (1350 to 2201)		

Statistical analyses

No statistical analyses for this end point

Secondary: GMTs Following Concomitant Administration of rMenB+OMV NZ with MenC-CRM or MenC-CRM Alone - Persistence

End point title	GMTs Following Concomitant Administration of rMenB+OMV NZ with MenC-CRM or MenC-CRM Alone - Persistence[11]

End point description:

Immunogenicity was assessed in terms of GMTs against N meningitidis serogroup C strain following co-administration of MenC-CRM and rMenB+OMV NZ or MenC-CRM alone at 3 and 5 months and booster dose at 12 months. Analysis was done on FAS-persistence.

End point type	Secondary

End point timeframe:

Pre-booster vaccination (persistence; 12 months of age)

Notes:

[11] - 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 null hypothesis associated with this immunogenicity objective.

End point values	BC_35_12	C_35_12		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	108	93		
Units: Titers				
geometric mean (confidence interval 95%)	36 (28 to 46)	56 (41 to 75)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentages of Subjects with hSBA Titers ≥ 4 or hSBA Titers ≥ 5 (M10713) and hSBA ≥ 8 Following Concomitant Administration of rMenB+OMV NZ with MenC-CRM

End point title	Percentages of Subjects with hSBA Titers ≥ 4 or hSBA Titers ≥ 5 (M10713) and hSBA ≥ 8 Following Concomitant Administration of rMenB+OMV NZ with MenC-CRM[12]

End point description:

Immunogenicity was assessed in terms of percentages of subjects with hSBA titers ≥ 4 against N meningitidis serogroup B strains H44/76, 5/99, NZ98/254; hSBA titers ≥ 5 against strain M10713; hSBA titers ≥ 8 against strains H44/76, 5/99, NZ98/254, M10713; following co-administration of MenC-CRM and rMenB+OMV NZ at 3 and 5 months and a booster at 12 months. Analysis was done on FAS-primary series and FAS-booster.

End point type	Secondary

End point timeframe:

1 month after second vaccination and 1 month after booster vaccination

Notes:

[12] - 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 null hypothesis associated with this immunogenicity objective.

End point values	BC_35_12			
Subject group type	Reporting group			
Number of subjects analysed	119			
Units: Percentage				
number (confidence interval 95%)				
H44/76 (hSBA≥4; 1 month after 2nd vacc)	97 (92 to 99)			
H44/76 (hSBA≥4; 1 month after booster vacc; N=114)	100 (97 to 100)			
5/99 (hSBA≥4; 1 month after 2nd vacc)	96 (90 to 99)			
5/99 (hSBA≥4; 1 month after booster vacc; N=113)	97 (92 to 99)			
NZ98/254 (hSBA≥4; 1 month after 2nd vacc; N=118)	95 (89 to 98)			
NZ98/254 (hSBA≥4; 1 mo after booster vacc; N=114)	97 (93 to 99)			
M10713 (hSBA≥5; 1 month after 2nd vacc; N=98)	68 (58 to 77)			
M10713 (hSBA≥5; 1 month after booster vacc; N=101)	67 (57 to 76)			
H44/76 (hSBA≥8; 1 month after 2nd vacc)	97 (92 to 99)			
H44/76 (hSBA≥8; 1 month after booster vacc; N=114)	99 (95 to 100)			
5/99 (hSBA≥8; 1 month after 2nd vacc)	96 (90 to 99)			

5/99 (hSBA≥8; 1 month after booster vacc; N=113)	97 (92 to 99)			
NZ98/254 (hSBA≥8; 1 month after 2nd vacc; N=118)	87 (80 to 93)			
NZ98/254 (hSBA≥8; 1 mo after booster vacc; N=114)	95 (89 to 98)			
M10713 (hSBA≥8; 1 month after 2nd vacc; N=98)	60 (50 to 70)			
M10713 (hSBA≥8; 1 month after booster vacc; N=101)	61 (51 to 71)			

Statistical analyses

No statistical analyses for this end point

Secondary: GMTs Against N. Meningitidis Serogroup B Strains Following Concomitant Administration of rMenB+OMV NZ with MenC-CRM

End point title	GMTs Against N. Meningitidis Serogroup B Strains Following Concomitant Administration of rMenB+OMV NZ with MenC-CRM[13]

End point description:

Immunogenicity was assessed in terms of GMTs against N meningitidis serogroup C strain following co-administration of MenC-CRM and rMenB+OMV NZ at 3 and 5 months and booster dose at 12 months. Analysis was done on FAS-persistence and FAS-booster.

End point type	Secondary

End point timeframe:

1 month after second vaccination, pre-booster vaccination and 1 month after booster vaccination

Notes:

[13] - 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 null hypothesis associated with this immunogenicity objective.

End point values	BC_35_12			
Subject group type	Reporting group			
Number of subjects analysed	115			
Units: Titers				
geometric mean (confidence interval 95%)				
H44/76 (1 month after 2nd vacc)	226 (179 to 284)			
H44/76 (Pre-booster vacc)	16 (13 to 20)			
H44/76 (1 month after booster vacc; N=114)	239 (198 to 288)			
5/99 (1 month after 2nd vacc)	555 (409 to 753)			
5/99 (Pre-booster vacc)	55 (42 to 72)			
5/99 (1 month after booster vacc; N=113)	1623 (1210 to 2176)			
NZ98/254 (1 month after 2nd vacc; N=114)	27 (21 to 34)			
NZ98/254 (Pre-booster vacc; N=115)	2.63 (2.21 to 3.14)			
NZ98/254 (1 month after booster vacc; N=114)	68 (54 to 86)			

M10713 (1 month after 2nd vacc; N=89)	9.81 (7.06 to 14)			
M10713 (Pre-booster vacc; N=110)	2.2 (1.72 to 2.82)			
M10713 (1 month after booster vacc; N=101)	11 (7.72 to 15)			

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean ELISA Concentrations Against Vaccine Antigen 287-953 Following Concomitant Administration of rMenB+OMV NZ with MenC-CRM

End point title	Geometric Mean ELISA Concentrations Against Vaccine Antigen 287-953 Following Concomitant Administration of rMenB+OMV NZ with MenC-CRM[14]

End point description:

Immunogenicity was assessed in terms of Geometric mean ELISA concentrations against N meningitidis serogroup B vaccine antigen 287-953, following co-administration of MenC-CRM and rMenB+OMV NZ at 3 and 5 months and booster dose at 12 months. Analysis was done on FAS-primary and FAS-booster.

End point type	Secondary

End point timeframe:

1 month after second vaccination, pre-booster vaccination and 1 month after booster vaccination

Notes:

[14] - 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 null hypothesis associated with this immunogenicity objective.

End point values	BC_35_12			
Subject group type	Reporting group			
Number of subjects analysed	116			
Units: IU/mL				
geometric mean (confidence interval 95%)				
1 month after 2nd vacc	2125 (1595 to 2830)			
Pre-booster vacc (N=111)	194 (164 to 230)			
1 month after booster vacc (N=113)	4281 (3411 to 5372)			

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean ELISA Concentrations Against Vaccine Antigen 287-953 Following Concomitant Administration of rMenB+OMV NZ with MenC-CRM - Persistence

End point title	Geometric Mean ELISA Concentrations Against Vaccine Antigen 287-953 Following Concomitant Administration of rMenB+OMV NZ with MenC-CRM - Persistence[15]

End point description:

Immunogenicity was assessed in terms of GMTs against Geometric mean ELISA concentrations against N meningitidis serogroup B vaccine antigen 287-953, following co-administration of MenC-CRM and rMenB+OMV NZ at 3 and 5 months and booster dose at 12 months. Analysis was done on FAS-persistence.

End point type	Secondary

End point timeframe:

Pre-booster vaccination (persistence; 12 months of age)

Notes:

[15] - 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 null hypothesis associated with this immunogenicity objective.

End point values	BC_35_12			
Subject group type	Reporting group			
Number of subjects analysed	115			
Units: IU/mL				
geometric mean (confidence interval 95%)	196 (166 to 231)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects who Reported Immediate Reactions within 30 Minutes after any Vaccination with rMenB+OMV NZ

End point title	Number of Subjects who Reported Immediate Reactions within 30 Minutes after any Vaccination with rMenB+OMV NZ

End point description:

Safety was assessed in terms of number of subjects who reported immediate reactions within 30 minutes following a 4-dose regimen (2.5, 3.5, 5 and 11 months) or a 3-dose regimen (3.5, 5 and 11 months or 6, 8 and 11 months) of rMenB+OMV NZ. Analysis was done on solicited safety set.

End point type	Secondary

End point timeframe:

Within 30 minutes after any vaccination

End point values	B_2h3h5_11b	B_3h5_11b	B_68_11b	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	252	249	250	
Units: Subjects				
Tenderness	13	9	9	
Erythema	19	19	7	
Induration	4	3	2	
Swelling	1	2	1	
Change in eating habits	0	2	1	
Sleepiness	1	2	3	
Unusual crying	4	3	4	
Vomiting	1	0	0	

Diarrhea	0	0	1	
Irritability	1	2	1	
Rash	0	1	1	
Fever (≥38°C)	3	2	2	
Medic. used for pain (N=252,248,250)	0	0	0	
Medically-attended fever	0	0	0	
Medic. used to treat high temp. (N=252,248,250)	1	1	0	
Medic. used to prevent high temp. (N=252,248,250)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Solicited Local and Systemic Adverse Events (AEs) Following a 3 or 4-dose Regimen of rMenB+OMV NZ

End point title	Number of Subjects with Solicited Local and Systemic Adverse Events (AEs) Following a 3 or 4-dose Regimen of rMenB+OMV NZ[16]

End point description:

Safety was assessed in terms of number of subjects with solicited local and systemic AEs after any vaccination following a 4-dose regimen (2.5, 3.5, 5 and 11 months) or as a 3-dose regimen (3.5, 5 and 11 months or 6, 8 and 11 months) of rMenB+OMV NZ. Analysis was done on solicited safety set.

End point type	Secondary

End point timeframe:

Day 1 to day 7 after any vaccination

Notes:

[16] - 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: All safety analyses were run in the safety population.

End point values	B_2h3h5_11	B_3h5_11	B_68_11	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	247	243	246	
Units: Subjects				
Any local (N=245,241,244)	226	213	202	
Tenderness (N=245,241,244)	200	174	166	
Erythema (N=245,241,244)	164	156	157	
Induration (N=245,241,244)	161	117	121	
Swelling (N=245,241,244)	120	75	84	
Any systemic (N=245,241,244)	238	236	233	
Change in eating habits (N=245,241,244)	141	112	121	
Sleepiness (N=245,241,244)	186	152	143	
Irritability (N=245,241,244)	180	156	151	
Vomiting (N=245,241,244)	65	39	55	
Diarrhea (N=245,241,244)	91	69	74	
Rash (N=245,241,244)	23	21	22	
Unusual Crying (N=245,241,244)	198	186	156	
Fever (≥38°C) (N=245,241,244)	197	189	184	

Medic. used for pain (N=245,241,244)	129	110	109	
Medic. used to prevent high temp. (N=245,241,244)	97	94	99	
Medic. used to treat high temp. (N=245,242,244)	193	186	177	
Medically-attended fever	16	10	15	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects who Reported Immediate Reactions within 30 Minutes After Any Vaccination - Groups B_02_2_5 and B_02_6_10

End point title	Number of Subjects who Reported Immediate Reactions within 30 Minutes After Any Vaccination - Groups B_02_2_5 and B_02_6_10[17]

End point description:

Safety was assessed in terms of number of subjects with solicited local and systemic AEs after any vaccination in subjects aged 2 - 10 years who received 2 catch-up doses of rMenB+OMV NZ, each at 0 and 2 months. Analysis was done on solicited safety set.

End point type	Secondary

End point timeframe:

Within 30 minutes after any vaccination

Notes:

[17] - 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 null hypothesis associated with this immunogenicity objective.

End point values	B_02_2_5	B_02_6_10		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	300		
Units: Subjects				
Pain	6	17		
Erythema	6	2		
Induration	1	3		
Swelling	2	2		
Chills (N=0,300)	0	2		
Change in eating habits (N=104,0)	0	0		
Sleepiness (N=104,0)	0	0		
Irritability (N=104,0)	1	0		
Vomiting (N=104,0)	0	0		
Nausea (N=0,300)	0	2		
Malaise (N=0,300)	0	4		
Diarrhoea (N=104,0)	0	0		
Headache	0	1		
Rash	0	0		
Arthralgia	0	1		
Myalgia (N=0,300)	0	5		
Fever (≥38°C)	0	0		
Medic. used for pain	0	1		

Medic. used to prevent high temp.	0	1		
Medic. used to treat high temp.	0	0		
Medically-attended fever	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Solicited Local and Systemic AEs in Groups B_02_2_5 and B_02_6_10

End point title	Number of Subjects with Solicited Local and Systemic AEs in Groups B_02_2_5 and B_02_6_10

End point description:

Safety was assessed in terms of number of subjects with solicited local and systemic AEs after any vaccination in subjects aged 2- 10 years who received 2 catch-up doses of rMenB+OMV NZ, each at 0 and 2 months. Analysis was done on solicited safety set.

End point type	Secondary

End point timeframe:

Day 1 to day 7 after any vaccination

End point values	B_02_2_5	B_02_6_10		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	102	299		
Units: Subjects				
Any Local (N=100,297)	99	287		
Pain (N=100,297)	98	287		
Erythema (N=100,297)	58	179		
Induration (N=100,297)	41	123		
Swelling (N=100,297)	50	146		
Any systemic (N=100,297)	78	205		
Chills (N=0,296)	0	45		
Change in eating habits (N=100,0)	35	0		
Sleepiness (N=100,0)	39	0		
Irritability (N=100,0)	49	0		
Malaise (N=0,296)	0	114		
Vomiting (N=100,0)	7	0		
Nausea (N=0,296)	0	36		
Diarrhoea (N=100,0)	12	0		
Headache (N=100,296)	7	89		
Rash (N=100,296)	9	20		
Arthralgia (N=100,296)	35	49		
Myalgia (N=0,296)	0	126		
Fever (≥38°C) (N=100,296)	20	41		
Medic. used for pain (N=100,296)	48	158		
Medic. used to prevent high temp. (N=100,296)	7	44		
Medic. used to treat high temp. (N=100,296)	20	54		

Medically-attended fever	0	7		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects who Reported Immediate Reactions Within 30 Minutes After Any rMenB+OMV NZ or MenC-CRM Vaccination

End point title	Number of Subjects who Reported Immediate Reactions Within 30 Minutes After Any rMenB+OMV NZ or MenC-CRM Vaccination[18]

End point description:

Safety was assessed in terms of number of subjects with solicited local and systemic AEs after any vaccination with rMenB+OMV NZ or MenC-CRM. Analysis was done on solicited safety set.

End point type	Secondary

End point timeframe:

Within 30 minutes after any vaccination

Notes:

[18] - 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: All safety analyses were run in the safety population.

End point values	BC_35_12	C_35_12		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	126	124		
Units: Subjects				
Tenderness (rMenB+OMV NZ) (N=126,0)	7	0		
Erythema (rMenB+OMV NZ) (N=126,0)	3	0		
Induration (rMenB+OMV NZ) (N=126,0)	1	0		
Swelling (rMenB+OMV NZ) (N=126,0)	0	0		
Tenderness (MenC-CRM)	5	5		
Erythema (MenC-CRM)	4	5		
Induration (MenC-CRM)	0	0		
Swelling (MenC-CRM)	0	0		
Change in eating habits	0	0		
Sleepiness	0	0		
Unusual crying	0	0		
Irritability	0	0		
Vomiting	1	0		
Diarrhea	0	0		
Rash	0	0		
Fever (≥38°C)	1	0		
Medic. used for pain	0	0		
Medic. used to prevent high temp.	0	0		
Medic. used to treat high temp.	0	0		
Medically-attended fever	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Solicited Local and Systemic AEs in Groups BC_35_12 and C_35_12 after any rMenB+OMV NZ or MenC-CRM Vaccination

End point title	Number of Subjects with Solicited Local and Systemic AEs in Groups BC_35_12 and C_35_12 after any rMenB+OMV NZ or MenC-CRM Vaccination[19]

End point description:

Safety was assessed in terms of number of subjects with solicited local and systemic AEs after any vaccination with rMenB+OMV NZ or MenC-CRM. Analysis was done on solicited safety set.

End point type	Secondary

End point timeframe:

Day 1 to day 7 after any vaccination

Notes:

[19] - 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: All safety analyses were run in the safety population.

End point values	BC_35_12	C_35_12		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	124	117		
Units: Subjects				
Any local rMenB + OMZ NV	107	0		
Any local MenC-CRM	104	79		
Any systemic	123	106		
Tenderness (rMenB+OMV NZ) (N=123,0)	105	0		
Erythema (rMenB+OMV NZ) (N=123,0)	48	0		
Induration (rMenB+OMV NZ) (N=123,0)	37	0		
Swelling (rMenB+OMV NZ) (N=123,0)	21	0		
Tenderness (MenC-CRM) (N=123,117)	104	74		
Erythema (MenC-CRM) (N=123,117)	25	24		
Induration (MenC-CRM) (N=123,117)	10	26		
Swelling (MenC-CRM) (N=123,117)	12	21		
Change in eating habits (N=123,117)	67	47		
Sleepiness (N=123,117)	93	78		
Unusual crying (N=123,117)	105	87		
Irritability (N=123,117)	95	66		
Vomiting (N=123,117)	29	27		
Diarrhea (N=123,117)	41	40		
Rash (N=123,117)	8	4		
Fever (≥38°C) (N=123,117)	97	45		
Medic. used for pain (N=123,117)	102	69		
Medic. used to prevent high temp.	49	25		

Medic. used to treat high temp.	90	40		
Medically-attended fever	7	12		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Reporting Unsolicited AEs Following Any Vaccination with rMenB+OMV NZ in Groups B_2h3h5_11, B_3h5_11 and B_68_11

End point title	Number of Subjects Reporting Unsolicited AEs Following Any Vaccination with rMenB+OMV NZ in Groups B_2h3h5_11, B_3h5_11 and B_68_11

End point description:

Safety was assessed in terms of number of subjects reporting any unsolicited AEs (day 1-7 after any vaccination), serious adverse events (SAEs), medically attended AEs, AEs leading to premature withdrawal from the study (collected throughout the study period) following any vaccination with rMenB+OMV. Analysis was done on unsolicited safety set.

End point type	Secondary

End point timeframe:

Until 12 months of age; Day 1 to day 7 (All AEs)

End point values	B_2h3h5_11b	B_3h5_11b	B_68_11b	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	252	249	250	
Units: Subjects				
All AEs (days 1-7)	200	186	196	
At least possible related AEs	88	41	62	
SAEs	15	18	9	
At least possibly related SAEs	1	1	1	
Medically attended AEs	178	179	182	
AEs leading to premature withdrawal	1	1	0	
Deaths	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Reporting Unsolicited AEs Following Any Vaccination with rMenB+OMV NZ in Groups B_02_2_5 and B_02_6_10

End point title	Number of Subjects Reporting Unsolicited AEs Following Any Vaccination with rMenB+OMV NZ in Groups B_02_2_5 and B_02_6_10[20]

End point description:

Safety was assessed in terms of number of subjects reporting any unsolicited AEs (day 1-7 after any vaccination), serious adverse events (SAEs), medically attended AEs, AEs leading to premature

withdrawal from the study (collected throughout the study period) following any vaccination with rMenB+OMV NZ. Analysis was done on unsolicited safety set.

End point type	Secondary

End point timeframe:

Day 1 to Day 7 (All AEs). Throughout the study period (SAEs, medically attended or leading to premature withdrawal AEs)

Notes:

[20] - 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: All safety analyses were run in the safety population.

End point values	B_02_2_5	B_02_6_10		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	300		
Units: Subjects				
All AEs (days 1-7)	58	101		
At least possible related AEs	16	24		
SAEs	1	2		
At least possibly related SAEs	0	0		
Medically attended AEs	42	74		
AEs leading to premature withdrawal	0	0		
Deaths	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Reporting Unsolicited AEs Following Any Vaccination with rMenB+OMV NZ in Group BC_35_12 and C_35_12

End point title	Number of Subjects Reporting Unsolicited AEs Following Any Vaccination with rMenB+OMV NZ in Group BC_35_12 and C_35_12[21]

End point description:

Safety was assessed in terms of number of subjects reporting any unsolicited AEs (day 1-7 after any vaccination), serious adverse events (SAEs), medically attended AEs, AEs leading to premature withdrawal from the study (collected throughout the study period) following any vaccination with rMenB+OMV NZ or MenC-CRM. Analysis was done on unsolicited safety set.

End point type	Secondary

End point timeframe:

Day 1 to Day 301 for BC_35_12 and C_35_12, Day 302 to Day 391 for C_35_12; Day 1 to day 7 (All AEs)

Notes:

[21] - 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: All safety analyses were run in the safety population.

End point values	BC_35_12	C_35_12		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	126	123		
Units: Subjects				
All AEs (days 1-7)	103	90		
At least possibly related AEs	14	12		
SAEs	5	7		
At least possibly related SAEs	0	0		
Medically attended AEs	99	85		
AEs leading to premature withdrawal	0	0		
Deaths	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 12 months of age for groups B_2h3h5_11, B_3h5_11 and B_68_11; Day 1 to Day 91 for groups B02_2_5 and B02_6_10; Day 1 to Day 301 for group BC_35_12; Day 1 to Day 391 for group C_35_12

Adverse event reporting additional description:

All solicited AEs were collected by systematic assessment and unsolicited AEs were collected by non-systematic assessment.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	B_68_11

Reporting group description:

Subjects, approximately 6 months of age received 2 dose primary vaccination of rMenB+OMV NZ at 6 and 8 months of age, followed by a booster dose at 11 months of age.

Reporting group title	B_3h5_11

Reporting group description:

Subjects, approximately 3.5 months of age received 2 dose primary vaccination of rMenB+OMV NZ at 3.5 and 5 months of age, followed by a booster dose at 11 months of age.

Reporting group title	B_2h3h5_11

Reporting group description:

Subjects, approximately 2.5 months of age received 3 dose primary vaccination of rMenB+OMV NZ at 2.5, 3.5, 5 months of age, followed by a booster dose at 11 months of age

Reporting group title	C_35_12

Reporting group description:

Subjects, 3 months of age received MenCCRM and Synflorix concomitantly at 3, 5 and 12 months of age and an additional dose of Synflorix alone at 7 months of age and rMenB+OMV NZ alone at 13 ad 15 months of age.

Reporting group title	BC_35_12

Reporting group description:

Subjects, 3 months of age received rMenB+OMV NZ + MenC-CRM and Synflorix concomitantly at 3, 5 and 12 months of age and an additional dose of Synflorix alone dose at 7 months of age

Reporting group title	B_02_6_10

Reporting group description:

Subjects, 6-10 years of age received 2 catch-up doses of rMenB+OMV NZ, each at 0 and 2 months. Blood draw at 0 and 3 months since study start.

Reporting group title	B_02_2_5

Reporting group description:

Subjects, 2-5 years of age received 2 catch-up doses of rMenB+OMV NZ, each at 0 and 2 months. Blood draw at 0 and 3 months since study start.

Serious adverse events	B_68_11	B_3h5_11	B_2h3h5_11
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 250 (3.60%)	18 / 249 (7.23%)	15 / 252 (5.95%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Injury, poisoning and procedural complications			
CONCUSSION			
subjects affected / exposed	0 / 250 (0.00%)	0 / 249 (0.00%)	0 / 252 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CONTUSION			
subjects affected / exposed	0 / 250 (0.00%)	0 / 249 (0.00%)	0 / 252 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FALL			
subjects affected / exposed	0 / 250 (0.00%)	0 / 249 (0.00%)	0 / 252 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SKULL FRACTURE			
subjects affected / exposed	0 / 250 (0.00%)	0 / 249 (0.00%)	1 / 252 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
CONGENITAL CENTRAL NERVOUS SYSTEM ANOMALY			
subjects affected / exposed	0 / 250 (0.00%)	0 / 249 (0.00%)	1 / 252 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
BENIGN INTRACRANIAL HYPERTENSION			
subjects affected / exposed	0 / 250 (0.00%)	0 / 249 (0.00%)	0 / 252 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FEBRILE CONVULSION			
subjects affected / exposed	0 / 250 (0.00%)	0 / 249 (0.00%)	0 / 252 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GENERALISED TONIC-CLONIC SEIZURE			

subjects affected / exposed	0 / 250 (0.00%)	0 / 249 (0.00%)	0 / 252 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 250 (0.00%)	2 / 249 (0.80%)	0 / 252 (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
LYMPHADENOPATHY			
subjects affected / exposed	1 / 250 (0.40%)	0 / 249 (0.00%)	0 / 252 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
PYREXIA			
subjects affected / exposed	1 / 250 (0.40%)	2 / 249 (0.80%)	2 / 252 (0.79%)
occurrences causally related to treatment / all	0 / 1	1 / 2	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
GLAUCOMA			
subjects affected / exposed	0 / 250 (0.00%)	0 / 249 (0.00%)	0 / 252 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
ALLERGIC COLITIS			
subjects affected / exposed	0 / 250 (0.00%)	1 / 249 (0.40%)	0 / 252 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIARRHOEA			
subjects affected / exposed	0 / 250 (0.00%)	1 / 249 (0.40%)	1 / 252 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FOOD POISONING			

subjects affected / exposed	0 / 250 (0.00%)	0 / 249 (0.00%)	0 / 252 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
INGUINAL HERNIA			
subjects affected / exposed	0 / 250 (0.00%)	0 / 249 (0.00%)	1 / 252 (0.40%)
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			
subjects affected / exposed	0 / 250 (0.00%)	1 / 249 (0.40%)	1 / 252 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
ADENOIDAL HYPERTROPHY			
subjects affected / exposed	0 / 250 (0.00%)	0 / 249 (0.00%)	0 / 252 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHOSPASM			
subjects affected / exposed	2 / 250 (0.80%)	0 / 249 (0.00%)	0 / 252 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
CHOKING			
subjects affected / exposed	0 / 250 (0.00%)	1 / 249 (0.40%)	0 / 252 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SLEEP APNOEA SYNDROME			
subjects affected / exposed	0 / 250 (0.00%)	0 / 249 (0.00%)	0 / 252 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TONSILLAR HYPERTROPHY			
subjects affected / exposed	0 / 250 (0.00%)	0 / 249 (0.00%)	0 / 252 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WHEEZING			

subjects affected / exposed	0 / 250 (0.00%)	1 / 249 (0.40%)	0 / 252 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
HYDRONEPHROSIS			
subjects affected / exposed	0 / 250 (0.00%)	0 / 249 (0.00%)	1 / 252 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
JUVENILE IDIOPATHIC ARTHRITIS			
subjects affected / exposed	1 / 250 (0.40%)	0 / 249 (0.00%)	0 / 252 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MUSCLE SPASMS			
subjects affected / exposed	0 / 250 (0.00%)	0 / 249 (0.00%)	1 / 252 (0.40%)
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			
ATYPICAL PNEUMONIA			
subjects affected / exposed	0 / 250 (0.00%)	0 / 249 (0.00%)	0 / 252 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHIOLITIS			
subjects affected / exposed	3 / 250 (1.20%)	2 / 249 (0.80%)	1 / 252 (0.40%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHITIS			
subjects affected / exposed	1 / 250 (0.40%)	2 / 249 (0.80%)	2 / 252 (0.79%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHOPNEUMONIA			
subjects affected / exposed	0 / 250 (0.00%)	1 / 249 (0.40%)	1 / 252 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

EAR INFECTION			
subjects affected / exposed	0 / 250 (0.00%)	1 / 249 (0.40%)	0 / 252 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROENTERITIS			
subjects affected / exposed	2 / 250 (0.80%)	4 / 249 (1.61%)	0 / 252 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROENTERITIS ROTAVIRUS			
subjects affected / exposed	0 / 250 (0.00%)	0 / 249 (0.00%)	0 / 252 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROENTERITIS SALMONELLA			
subjects affected / exposed	0 / 250 (0.00%)	1 / 249 (0.40%)	0 / 252 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LARYNGITIS			
subjects affected / exposed	1 / 250 (0.40%)	0 / 249 (0.00%)	2 / 252 (0.79%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 250 (0.00%)	1 / 249 (0.40%)	0 / 252 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MASTOIDITIS			
subjects affected / exposed	0 / 250 (0.00%)	1 / 249 (0.40%)	0 / 252 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NASOPHARYNGITIS			
subjects affected / exposed	0 / 250 (0.00%)	0 / 249 (0.00%)	0 / 252 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ORAL CANDIDIASIS			

subjects affected / exposed	0 / 250 (0.00%)	1 / 249 (0.40%)	0 / 252 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA			
subjects affected / exposed	1 / 250 (0.40%)	2 / 249 (0.80%)	1 / 252 (0.40%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PYELONEPHRITIS			
subjects affected / exposed	0 / 250 (0.00%)	0 / 249 (0.00%)	1 / 252 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY SYNCYTIAL VIRUS BRONCHIOLITIS			
subjects affected / exposed	0 / 250 (0.00%)	0 / 249 (0.00%)	2 / 252 (0.79%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY TRACT INFECTION VIRAL			
subjects affected / exposed	1 / 250 (0.40%)	0 / 249 (0.00%)	0 / 252 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SALMONELLOSIS			
subjects affected / exposed	0 / 250 (0.00%)	1 / 249 (0.40%)	0 / 252 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	1 / 250 (0.40%)	0 / 249 (0.00%)	0 / 252 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION			
subjects affected / exposed	0 / 250 (0.00%)	1 / 249 (0.40%)	1 / 252 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			

COW'S MILK INTOLERANCE			
subjects affected / exposed	0 / 250 (0.00%)	1 / 249 (0.40%)	0 / 252 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEHYDRATION			
subjects affected / exposed	0 / 250 (0.00%)	3 / 249 (1.20%)	1 / 252 (0.40%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	C_35_12	BC_35_12	B_02_6_10
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 123 (6.50%)	5 / 126 (3.97%)	2 / 300 (0.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
CONCUSSION			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	1 / 300 (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
CONTUSION			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	1 / 300 (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
FALL			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	1 / 300 (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
SKULL FRACTURE			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
CONGENITAL CENTRAL NERVOUS SYSTEM ANOMALY			

subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
BENIGN INTRACRANIAL HYPERTENSION			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	1 / 300 (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
FEBRILE CONVULSION			
subjects affected / exposed	1 / 123 (0.81%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GENERALISED TONIC-CLONIC SEIZURE			
subjects affected / exposed	1 / 123 (0.81%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LYMPHADENOPATHY			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
PYREXIA			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
GLAUCOMA			

subjects affected / exposed	1 / 123 (0.81%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
ALLERGIC COLITIS			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DIARRHOEA			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
FOOD POISONING			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	1 / 300 (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
INGUINAL HERNIA			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
VOMITING			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
ADENOIDAL HYPERTROPHY			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHOSPASM			
subjects affected / exposed	1 / 123 (0.81%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

CHOKING			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SLEEP APNOEA SYNDROME			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
TONSILLAR HYPERTROPHY			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
WHEEZING			
subjects affected / exposed	0 / 123 (0.00%)	1 / 126 (0.79%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
HYDRONEPHROSIS			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
JUVENILE IDIOPATHIC ARTHRITIS			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MUSCLE SPASMS			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
ATYPICAL PNEUMONIA			

subjects affected / exposed	0 / 123 (0.00%)	1 / 126 (0.79%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHIOLITIS			
subjects affected / exposed	1 / 123 (0.81%)	2 / 126 (1.59%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHITIS			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
BRONCHOPNEUMONIA			
subjects affected / exposed	3 / 123 (2.44%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
EAR INFECTION			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROENTERITIS			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROENTERITIS ROTAVIRUS			
subjects affected / exposed	1 / 123 (0.81%)	1 / 126 (0.79%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
GASTROENTERITIS SALMONELLA			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LARYNGITIS			

subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
MASTOIDITIS			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
NASOPHARYNGITIS			
subjects affected / exposed	0 / 123 (0.00%)	1 / 126 (0.79%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ORAL CANDIDIASIS			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
PNEUMONIA			
subjects affected / exposed	0 / 123 (0.00%)	2 / 126 (1.59%)	0 / 300 (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
PYELONEPHRITIS			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY SYNCYTIAL VIRUS BRONCHIOLITIS			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
RESPIRATORY TRACT INFECTION VIRAL			

subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
SALMONELLOSIS			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
URINARY TRACT INFECTION			
subjects affected / exposed	1 / 123 (0.81%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
COW'S MILK INTOLERANCE			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
DEHYDRATION			
subjects affected / exposed	1 / 123 (0.81%)	0 / 126 (0.00%)	0 / 300 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	B_02_2_5		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 104 (0.96%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
CONCUSSION			

subjects affected / exposed	0 / 104 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CONTUSION				
subjects affected / exposed	0 / 104 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
FALL				
subjects affected / exposed	0 / 104 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SKULL FRACTURE				
subjects affected / exposed	0 / 104 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Congenital, familial and genetic disorders				
CONGENITAL CENTRAL NERVOUS SYSTEM ANOMALY				
subjects affected / exposed	0 / 104 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
BENIGN INTRACRANIAL HYPERTENSION				
subjects affected / exposed	0 / 104 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
FEBRILE CONVULSION				
subjects affected / exposed	0 / 104 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
GENERALISED TONIC-CLONIC SEIZURE				

subjects affected / exposed	0 / 104 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
ANAEMIA			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
LYMPHADENOPATHY			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
PYREXIA			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
GLAUCOMA			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
ALLERGIC COLITIS			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
DIARRHOEA			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
FOOD POISONING			

subjects affected / exposed	0 / 104 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
INGUINAL HERNIA				
subjects affected / exposed	0 / 104 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
VOMITING				
subjects affected / exposed	0 / 104 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
ADENOIDAL HYPERTROPHY				
subjects affected / exposed	1 / 104 (0.96%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
BRONCHOSPASM				
subjects affected / exposed	0 / 104 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
CHOKING				
subjects affected / exposed	0 / 104 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SLEEP APNOEA SYNDROME				
subjects affected / exposed	1 / 104 (0.96%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
TONSILLAR HYPERTROPHY				
subjects affected / exposed	1 / 104 (0.96%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
WHEEZING				

subjects affected / exposed	0 / 104 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
HYDRONEPHROSIS			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
JUVENILE IDIOPATHIC ARTHRITIS			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
MUSCLE SPASMS			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
ATYPICAL PNEUMONIA			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
BRONCHIOLITIS			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
BRONCHITIS			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
BRONCHOPNEUMONIA			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

EAR INFECTION			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
GASTROENTERITIS			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
GASTROENTERITIS ROTAVIRUS			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
GASTROENTERITIS SALMONELLA			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
LARYNGITIS			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
LOWER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
MASTOIDITIS			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
NASOPHARYNGITIS			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
ORAL CANDIDIASIS			

subjects affected / exposed	0 / 104 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PNEUMONIA				
subjects affected / exposed	0 / 104 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
PYELONEPHRITIS				
subjects affected / exposed	0 / 104 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
RESPIRATORY SYNCYTIAL VIRUS BRONCHIOLITIS				
subjects affected / exposed	0 / 104 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
RESPIRATORY TRACT INFECTION VIRAL				
subjects affected / exposed	0 / 104 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
SALMONELLOSIS				
subjects affected / exposed	0 / 104 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
UPPER RESPIRATORY TRACT INFECTION				
subjects affected / exposed	0 / 104 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
URINARY TRACT INFECTION				
subjects affected / exposed	0 / 104 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				

COW'S MILK INTOLERANCE			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
DEHYDRATION			
subjects affected / exposed	0 / 104 (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	B_68_11	B_3h5_11	B_2h3h5_11
Total subjects affected by non-serious adverse events			
subjects affected / exposed	245 / 250 (98.00%)	240 / 249 (96.39%)	246 / 252 (97.62%)
Nervous system disorders			
HEADACHE			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 250 (0.00%)	0 / 249 (0.00%)	0 / 252 (0.00%)
occurrences (all)	0	0	0
SOMNOLENCE			
alternative assessment type: Systematic			
subjects affected / exposed	144 / 250 (57.60%)	152 / 249 (61.04%)	186 / 252 (73.81%)
occurrences (all)	256	296	450
General disorders and administration site conditions			
CHILLS			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 250 (0.00%)	0 / 249 (0.00%)	0 / 252 (0.00%)
occurrences (all)	0	0	0
CRYING			
alternative assessment type: Systematic			
subjects affected / exposed	157 / 250 (62.80%)	186 / 249 (74.70%)	198 / 252 (78.57%)
occurrences (all)	333	350	554
INDURATION			
alternative assessment type: Systematic			

subjects affected / exposed	27 / 250 (10.80%)	23 / 249 (9.24%)	58 / 252 (23.02%)
occurrences (all)	42	33	101
INJECTION SITE ERYTHEMA			
alternative assessment type: Systematic			
subjects affected / exposed	157 / 250 (62.80%)	160 / 249 (64.26%)	169 / 252 (67.06%)
occurrences (all)	314	312	427
INJECTION SITE INDURATION			
alternative assessment type: Systematic			
subjects affected / exposed	122 / 250 (48.80%)	118 / 249 (47.39%)	162 / 252 (64.29%)
occurrences (all)	227	209	382
INJECTION SITE PAIN			
alternative assessment type: Systematic			
subjects affected / exposed	168 / 250 (67.20%)	175 / 249 (70.28%)	202 / 252 (80.16%)
occurrences (all)	348	340	505
INJECTION SITE SWELLING			
alternative assessment type: Systematic			
subjects affected / exposed	84 / 250 (33.60%)	76 / 249 (30.52%)	120 / 252 (47.62%)
occurrences (all)	137	110	237
MALAISE			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 250 (0.00%)	0 / 249 (0.00%)	0 / 252 (0.00%)
occurrences (all)	0	0	0
PYREXIA			
alternative assessment type: Systematic			
subjects affected / exposed	189 / 250 (75.60%)	192 / 249 (77.11%)	201 / 252 (79.76%)
occurrences (all)	429	403	505
SWELLING			
alternative assessment type: Systematic			
subjects affected / exposed	19 / 250 (7.60%)	6 / 249 (2.41%)	26 / 252 (10.32%)
occurrences (all)	20	6	36
Gastrointestinal disorders			
DIARRHOEA			
alternative assessment type: Systematic			

subjects affected / exposed	76 / 250 (30.40%)	74 / 249 (29.72%)	96 / 252 (38.10%)
occurrences (all)	134	108	172
NAUSEA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 250 (0.00%)	0 / 249 (0.00%)	0 / 252 (0.00%)
occurrences (all)	0	0	0
VOMITING			
alternative assessment type: Systematic			
subjects affected / exposed	58 / 250 (23.20%)	46 / 249 (18.47%)	69 / 252 (27.38%)
occurrences (all)	93	60	110
Respiratory, thoracic and mediastinal disorders			
BRONCHOSPASM			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 250 (1.20%)	5 / 249 (2.01%)	3 / 252 (1.19%)
occurrences (all)	5	5	4
CATARRH			
alternative assessment type: Systematic			
subjects affected / exposed	14 / 250 (5.60%)	14 / 249 (5.62%)	8 / 252 (3.17%)
occurrences (all)	19	15	14
COUGH			
alternative assessment type: Systematic			
subjects affected / exposed	13 / 250 (5.20%)	6 / 249 (2.41%)	12 / 252 (4.76%)
occurrences (all)	18	6	15
Skin and subcutaneous tissue disorders			
ERYTHEMA			
alternative assessment type: Systematic			
subjects affected / exposed	12 / 250 (4.80%)	8 / 249 (3.21%)	20 / 252 (7.94%)
occurrences (all)	18	11	29
RASH			
alternative assessment type: Systematic			
subjects affected / exposed	32 / 250 (12.80%)	28 / 249 (11.24%)	36 / 252 (14.29%)
occurrences (all)	42	31	51
Psychiatric disorders			

EATING DISORDER			
alternative assessment type: Systematic			
subjects affected / exposed	121 / 250 (48.40%)	112 / 249 (44.98%)	141 / 252 (55.95%)
occurrences (all)	242	188	302
IRRITABILITY			
alternative assessment type: Systematic			
subjects affected / exposed	153 / 250 (61.20%)	156 / 249 (62.65%)	181 / 252 (71.83%)
occurrences (all)	317	312	478
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 250 (0.00%)	0 / 249 (0.00%)	0 / 252 (0.00%)
occurrences (all)	0	0	0
MYALGIA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 250 (0.00%)	0 / 249 (0.00%)	0 / 252 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
BRONCHIOLITIS			
alternative assessment type: Systematic			
subjects affected / exposed	13 / 250 (5.20%)	26 / 249 (10.44%)	18 / 252 (7.14%)
occurrences (all)	14	29	26
BRONCHITIS			
alternative assessment type: Systematic			
subjects affected / exposed	33 / 250 (13.20%)	36 / 249 (14.46%)	37 / 252 (14.68%)
occurrences (all)	51	53	54
BRONCHOPNEUMONIA			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 250 (0.40%)	2 / 249 (0.80%)	0 / 252 (0.00%)
occurrences (all)	1	2	0
CONJUNCTIVITIS			
alternative assessment type: Systematic			
subjects affected / exposed	17 / 250 (6.80%)	15 / 249 (6.02%)	27 / 252 (10.71%)
occurrences (all)	19	16	30
EAR INFECTION			

alternative assessment type: Systematic			
subjects affected / exposed	16 / 250 (6.40%)	9 / 249 (3.61%)	12 / 252 (4.76%)
occurrences (all)	21	9	13
GASTROENTERITIS			
alternative assessment type: Systematic			
subjects affected / exposed	32 / 250 (12.80%)	23 / 249 (9.24%)	25 / 252 (9.92%)
occurrences (all)	37	25	31
INFLUENZA			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 250 (2.00%)	4 / 249 (1.61%)	7 / 252 (2.78%)
occurrences (all)	6	5	8
LARYNGITIS			
alternative assessment type: Systematic			
subjects affected / exposed	15 / 250 (6.00%)	5 / 249 (2.01%)	12 / 252 (4.76%)
occurrences (all)	17	5	12
NASOPHARYNGITIS			
alternative assessment type: Systematic			
subjects affected / exposed	47 / 250 (18.80%)	31 / 249 (12.45%)	38 / 252 (15.08%)
occurrences (all)	71	55	73
OTITIS MEDIA			
alternative assessment type: Systematic			
subjects affected / exposed	14 / 250 (5.60%)	4 / 249 (1.61%)	7 / 252 (2.78%)
occurrences (all)	17	4	9
OTITIS MEDIA ACUTE			
alternative assessment type: Systematic			
subjects affected / exposed	14 / 250 (5.60%)	8 / 249 (3.21%)	10 / 252 (3.97%)
occurrences (all)	15	10	12
PHARYNGITIS			
alternative assessment type: Systematic			
subjects affected / exposed	14 / 250 (5.60%)	10 / 249 (4.02%)	11 / 252 (4.37%)
occurrences (all)	16	12	12
RESPIRATORY TRACT INFECTION			
alternative assessment type: Systematic			

subjects affected / exposed	28 / 250 (11.20%)	14 / 249 (5.62%)	18 / 252 (7.14%)
occurrences (all)	37	26	30
TONSILLITIS			
alternative assessment type: Systematic			
subjects affected / exposed	7 / 250 (2.80%)	3 / 249 (1.20%)	6 / 252 (2.38%)
occurrences (all)	10	3	7
UPPER RESPIRATORY TRACT INFECTION			
alternative assessment type: Systematic			
subjects affected / exposed	54 / 250 (21.60%)	56 / 249 (22.49%)	49 / 252 (19.44%)
occurrences (all)	79	86	67
VIRAL INFECTION			
alternative assessment type: Systematic			
subjects affected / exposed	14 / 250 (5.60%)	26 / 249 (10.44%)	16 / 252 (6.35%)
occurrences (all)	15	32	21

Non-serious adverse events	C_35_12	BC_35_12	B_02_6_10
Total subjects affected by non-serious adverse events			
subjects affected / exposed	115 / 123 (93.50%)	124 / 126 (98.41%)	288 / 300 (96.00%)
Nervous system disorders			
HEADACHE			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	90 / 300 (30.00%)
occurrences (all)	0	0	124
SOMNOLENCE			
alternative assessment type: Systematic			
subjects affected / exposed	84 / 123 (68.29%)	93 / 126 (73.81%)	0 / 300 (0.00%)
occurrences (all)	233	214	0
General disorders and administration site conditions			
CHILLS			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	47 / 300 (15.67%)
occurrences (all)	0	0	51
CRYING			
alternative assessment type: Systematic			

subjects affected / exposed	93 / 123 (75.61%)	105 / 126 (83.33%)	0 / 300 (0.00%)
occurrences (all)	289	271	0
INDURATION			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 123 (0.81%)	1 / 126 (0.79%)	6 / 300 (2.00%)
occurrences (all)	1	1	6
INJECTION SITE ERYTHEMA			
alternative assessment type: Systematic			
subjects affected / exposed	41 / 123 (33.33%)	62 / 126 (49.21%)	180 / 300 (60.00%)
occurrences (all)	142	197	272
INJECTION SITE INDURATION			
alternative assessment type: Systematic			
subjects affected / exposed	41 / 123 (33.33%)	42 / 126 (33.33%)	124 / 300 (41.33%)
occurrences (all)	107	107	173
INJECTION SITE PAIN			
alternative assessment type: Systematic			
subjects affected / exposed	102 / 123 (82.93%)	114 / 126 (90.48%)	287 / 300 (95.67%)
occurrences (all)	469	685	537
INJECTION SITE SWELLING			
alternative assessment type: Systematic			
subjects affected / exposed	35 / 123 (28.46%)	34 / 126 (26.98%)	146 / 300 (48.67%)
occurrences (all)	96	76	218
MALAISE			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	117 / 300 (39.00%)
occurrences (all)	0	0	160
PYREXIA			
alternative assessment type: Systematic			
subjects affected / exposed	77 / 123 (62.60%)	99 / 126 (78.57%)	47 / 300 (15.67%)
occurrences (all)	162	195	56
SWELLING			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	4 / 300 (1.33%)
occurrences (all)	0	0	4

Gastrointestinal disorders			
DIARRHOEA			
alternative assessment type: Systematic			
subjects affected / exposed	49 / 123 (39.84%)	41 / 126 (32.54%)	5 / 300 (1.67%)
occurrences (all)	99	61	5
NAUSEA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	38 / 300 (12.67%)
occurrences (all)	0	0	44
VOMITING			
alternative assessment type: Systematic			
subjects affected / exposed	31 / 123 (25.20%)	30 / 126 (23.81%)	6 / 300 (2.00%)
occurrences (all)	48	44	6
Respiratory, thoracic and mediastinal disorders			
BRONCHOSPASM			
alternative assessment type: Systematic			
subjects affected / exposed	7 / 123 (5.69%)	8 / 126 (6.35%)	0 / 300 (0.00%)
occurrences (all)	13	9	0
CATARRH			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	2 / 300 (0.67%)
occurrences (all)	0	0	2
COUGH			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 123 (0.81%)	1 / 126 (0.79%)	5 / 300 (1.67%)
occurrences (all)	1	1	5
Skin and subcutaneous tissue disorders			
ERYTHEMA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 123 (0.00%)	2 / 126 (1.59%)	3 / 300 (1.00%)
occurrences (all)	0	2	4
RASH			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 123 (4.88%)	11 / 126 (8.73%)	21 / 300 (7.00%)
occurrences (all)	7	13	23

Psychiatric disorders			
EATING DISORDER			
alternative assessment type: Systematic			
subjects affected / exposed	64 / 123 (52.03%)	67 / 126 (53.17%)	0 / 300 (0.00%)
occurrences (all)	145	119	0
IRRITABILITY			
alternative assessment type: Systematic			
subjects affected / exposed	79 / 123 (64.23%)	95 / 126 (75.40%)	1 / 300 (0.33%)
occurrences (all)	231	237	1
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	50 / 300 (16.67%)
occurrences (all)	0	0	63
MYALGIA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	127 / 300 (42.33%)
occurrences (all)	0	0	169
Infections and infestations			
BRONCHIOLITIS			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 123 (4.07%)	6 / 126 (4.76%)	0 / 300 (0.00%)
occurrences (all)	5	6	0
BRONCHITIS			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 123 (2.44%)	0 / 126 (0.00%)	7 / 300 (2.33%)
occurrences (all)	3	0	7
BRONCHOPNEUMONIA			
alternative assessment type: Systematic			
subjects affected / exposed	9 / 123 (7.32%)	6 / 126 (4.76%)	0 / 300 (0.00%)
occurrences (all)	11	8	0
CONJUNCTIVITIS			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 123 (2.44%)	2 / 126 (1.59%)	1 / 300 (0.33%)
occurrences (all)	3	2	1

EAR INFECTION			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 123 (4.07%)	1 / 126 (0.79%)	0 / 300 (0.00%)
occurrences (all)	5	1	0
GASTROENTERITIS			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 123 (4.88%)	5 / 126 (3.97%)	3 / 300 (1.00%)
occurrences (all)	6	6	3
INFLUENZA			
alternative assessment type: Systematic			
subjects affected / exposed	2 / 123 (1.63%)	7 / 126 (5.56%)	3 / 300 (1.00%)
occurrences (all)	2	7	3
LARYNGITIS			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 123 (0.00%)	3 / 126 (2.38%)	0 / 300 (0.00%)
occurrences (all)	0	3	0
NASOPHARYNGITIS			
alternative assessment type: Systematic			
subjects affected / exposed	11 / 123 (8.94%)	14 / 126 (11.11%)	5 / 300 (1.67%)
occurrences (all)	16	17	5
OTITIS MEDIA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 123 (0.00%)	0 / 126 (0.00%)	2 / 300 (0.67%)
occurrences (all)	0	0	2
OTITIS MEDIA ACUTE			
alternative assessment type: Systematic			
subjects affected / exposed	16 / 123 (13.01%)	12 / 126 (9.52%)	0 / 300 (0.00%)
occurrences (all)	20	15	0
PHARYNGITIS			
alternative assessment type: Systematic			
subjects affected / exposed	10 / 123 (8.13%)	6 / 126 (4.76%)	4 / 300 (1.33%)
occurrences (all)	10	6	4
RESPIRATORY TRACT INFECTION			
alternative assessment type: Systematic			

subjects affected / exposed	3 / 123 (2.44%)	3 / 126 (2.38%)	0 / 300 (0.00%)
occurrences (all)	3	3	0
TONSILLITIS			
alternative assessment type: Systematic			
subjects affected / exposed	12 / 123 (9.76%)	6 / 126 (4.76%)	2 / 300 (0.67%)
occurrences (all)	12	6	2
UPPER RESPIRATORY TRACT INFECTION			
alternative assessment type: Systematic			
subjects affected / exposed	60 / 123 (48.78%)	59 / 126 (46.83%)	6 / 300 (2.00%)
occurrences (all)	110	87	6
VIRAL INFECTION			
alternative assessment type: Systematic			
subjects affected / exposed	10 / 123 (8.13%)	11 / 126 (8.73%)	4 / 300 (1.33%)
occurrences (all)	11	11	6

Non-serious adverse events	B_02_2_5		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	100 / 104 (96.15%)		
Nervous system disorders			
HEADACHE			
alternative assessment type: Systematic			
subjects affected / exposed	7 / 104 (6.73%)		
occurrences (all)	8		
SOMNOLENCE			
alternative assessment type: Systematic			
subjects affected / exposed	39 / 104 (37.50%)		
occurrences (all)	51		
General disorders and administration site conditions			
CHILLS			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences (all)	0		
CRYING			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 104 (0.00%)			
occurrences (all)	0			
INDURATION				
alternative assessment type: Systematic				
subjects affected / exposed	7 / 104 (6.73%)			
occurrences (all)	8			
INJECTION SITE ERYTHEMA				
alternative assessment type: Systematic				
subjects affected / exposed	59 / 104 (56.73%)			
occurrences (all)	94			
INJECTION SITE INDURATION				
alternative assessment type: Systematic				
subjects affected / exposed	41 / 104 (39.42%)			
occurrences (all)	63			
INJECTION SITE PAIN				
alternative assessment type: Systematic				
subjects affected / exposed	99 / 104 (95.19%)			
occurrences (all)	183			
INJECTION SITE SWELLING				
alternative assessment type: Systematic				
subjects affected / exposed	50 / 104 (48.08%)			
occurrences (all)	73			
MALAISE				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 104 (0.00%)			
occurrences (all)	0			
PYREXIA				
alternative assessment type: Systematic				
subjects affected / exposed	22 / 104 (21.15%)			
occurrences (all)	27			
SWELLING				
alternative assessment type: Systematic				
subjects affected / exposed	6 / 104 (5.77%)			
occurrences (all)	6			

Gastrointestinal disorders			
DIARRHOEA			
alternative assessment type: Systematic			
subjects affected / exposed	12 / 104 (11.54%)		
occurrences (all)	15		
NAUSEA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences (all)	0		
VOMITING			
alternative assessment type: Systematic			
subjects affected / exposed	8 / 104 (7.69%)		
occurrences (all)	12		
Respiratory, thoracic and mediastinal disorders			
BRONCHOSPASM			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences (all)	0		
CATARRH			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences (all)	0		
COUGH			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 104 (2.88%)		
occurrences (all)	3		
Skin and subcutaneous tissue disorders			
ERYTHEMA			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 104 (5.77%)		
occurrences (all)	6		
RASH			
alternative assessment type: Systematic			
subjects affected / exposed	9 / 104 (8.65%)		
occurrences (all)	9		

Psychiatric disorders			
EATING DISORDER			
alternative assessment type: Systematic			
subjects affected / exposed	35 / 104 (33.65%)		
occurrences (all)	50		
IRRITABILITY			
alternative assessment type: Systematic			
subjects affected / exposed	49 / 104 (47.12%)		
occurrences (all)	75		
Musculoskeletal and connective tissue disorders			
ARTHRALGIA			
alternative assessment type: Systematic			
subjects affected / exposed	35 / 104 (33.65%)		
occurrences (all)	47		
MYALGIA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences (all)	0		
Infections and infestations			
BRONCHIOLITIS			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences (all)	0		
BRONCHITIS			
alternative assessment type: Systematic			
subjects affected / exposed	6 / 104 (5.77%)		
occurrences (all)	6		
BRONCHOPNEUMONIA			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences (all)	0		
CONJUNCTIVITIS			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 104 (0.00%)		
occurrences (all)	0		

EAR INFECTION				
alternative assessment type: Systematic				
subjects affected / exposed	3 / 104 (2.88%)			
occurrences (all)	3			
GASTROENTERITIS				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 104 (0.96%)			
occurrences (all)	1			
INFLUENZA				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 104 (0.00%)			
occurrences (all)	0			
LARYNGITIS				
alternative assessment type: Systematic				
subjects affected / exposed	0 / 104 (0.00%)			
occurrences (all)	0			
NASOPHARYNGITIS				
alternative assessment type: Systematic				
subjects affected / exposed	5 / 104 (4.81%)			
occurrences (all)	6			
OTITIS MEDIA				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 104 (0.96%)			
occurrences (all)	1			
OTITIS MEDIA ACUTE				
alternative assessment type: Systematic				
subjects affected / exposed	1 / 104 (0.96%)			
occurrences (all)	2			
PHARYNGITIS				
alternative assessment type: Systematic				
subjects affected / exposed	2 / 104 (1.92%)			
occurrences (all)	2			
RESPIRATORY TRACT INFECTION				
alternative assessment type: Systematic				

subjects affected / exposed	0 / 104 (0.00%)		
occurrences (all)	0		
TONSILLITIS			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 104 (0.96%)		
occurrences (all)	1		
UPPER RESPIRATORY TRACT INFECTION			
alternative assessment type: Systematic			
subjects affected / exposed	3 / 104 (2.88%)		
occurrences (all)	4		
VIRAL INFECTION			
alternative assessment type: Systematic			
subjects affected / exposed	4 / 104 (3.85%)		
occurrences (all)	4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 May 2011	Alignment of the protocol with the actual SAE notification and reporting process
20 February 2012	New arms to test concomitant MenB + MenC administration
29 August 2013	hSBA cut-off adjustement following serological test outsource
26 November 2013	Inclusion of an interim analysis on a subset of subjects in Group II - End of trial definition

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported