Clinical trial results:
A Phase 2b, Open Label, Randomized, Parallel-Group, Multi-Center Study to Evaluate the Safety, Tolerability and Immunogenicity of Novartis Meningococcal B Recombinant Vaccine When Administered with or without Routine Infant Vaccinations to Healthy Infants According to Different Immunization Schedules

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

Summary

EudraCT number	2008-001592-30
Trial protocol	GB DE ES IT BE CZ
Global end of trial date	02 July 2010

Results information

Result version number	v2 (current)
This version publication date	04 June 2016
First version publication date	07 January 2015
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	V72P12

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00721396
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000139-PIP01-07
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	24 September 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 July 2010
Global end of trial reached?	Yes
Global end of trial date	02 July 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary :1.To demonstrate a sufficient immune response of rMenB+OMV NZ, when given concomitantly with routine infant vaccines to healthy infants at 2, 4 and 6 and 2, 3 and 4 months of age, as measured by percentage of subjects with serum bactericidal activity (SBA) titer ≥1:5, at 1 month after the third vaccination
Secondary :To demonstrate that immunogenicity of routine infant vaccines, when given concomitantly with rMenB+OMV NZ to healthy infants at 2, 3 and 4 months of age, was non-inferior to that of routine infant vaccines given without rMenB+OMV NZ. 2. To demonstrate that the immunogenicity of rMenB+OMV NZ when given concomitantly with routine infant vaccines was non-inferior to that of rMenB+OMV NZ given without routine infant vaccines at 2, 4 and 6 months of age. 3. To assess prevalence of meningococcal B antibodies over the study period by evaluation of SBA, at baseline and at 1 month after third vaccination, in subjects- received routine infant vaccine without rMenB+OMV NZ

Protection of trial subjects:

Novartis Vaccines or the investigator provided the ethics committee (EC) with all appropriate material,including the Informed Consent Form (ICF), according to local regulations. The EC also was asked for a written statement regarding the composition of the committee and to comply with GCP (Good Clinical Practices) and with the applicable regulatory requirement(s). The trial was not initiated until appropriate EC approval of the protocol and the ICF was obtained. In addition, all documents were submitted to other authorities in compliance with local jurisdictions. Prior to enrollment, the sponsor and the investigator exchanged written confirmation that their ethical and legal responsibilities had been observed. The EC and, if applicable, other authorities were informed of protocol amendments in accordance with local legal requirements. Appropriate reports on the progress of the study were made to the EC and the sponsor by the investigator in accordance with applicable governmental regulations and in agreement with policy established by the sponsor.

Background therapy:

The Novartis meningococcal B recombinant vaccine (rMenB + OMV), was supplied as 0.5mL dose in pre-filled syringes and administered by intramuscular (IM) injection into the anterolateral region of the right thigh. The active ingredients were 50µg of each of the following N. meningitidis purified antigens: 961c, 936-741, ΔG287-953. In addition, 25 µg OMV from N. meningitidis strain NZ98/254. Routine vaccines (Infanrix® Hexa and Prevenar®) were administered along with the study vaccine where appropriate.

Evidence for comparator:

There was no reference vaccine in this study

Actual start date of recruitment	15 August 2008
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 317
Country: Number of subjects enrolled	Belgium: 248
Country: Number of subjects enrolled	Czech Republic: 283
Country: Number of subjects enrolled	Italy: 371
Country: Number of subjects enrolled	Spain: 105
Country: Number of subjects enrolled	United Kingdom: 561
Worldwide total number of subjects	1885
EEA total number of subjects	1885

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)	1885
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited from 4 centers in UK, 5 centers in Italy, 16 centers in Spain, 6 centers in Belgium, 25 centers in Germany and 4 centers in Czech Republic

Pre-assignment

Screening details:

All subjects enrolled were included in the trial

Period 1

Period 1 title	overall (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+R246

Arm description:

Subjects in this group received rMenB+OMV NZ vaccine at 2, 4, and 6 months of age, administered concomitantly with routine infant vaccinations

Arm type	Active comparator
Investigational medicinal product name	Novartis Meningococcal B Recombinant Vaccine
Investigational medicinal product code	V72
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5mL/1 dose

Arm title	B246_R357

Arm description:

Subjects in this group received rMenB+OMV NZ vaccine at 2, 4, and 6 months of age; routine infant vaccinations were administered at 3, 5 and 7 months of age

Arm type	Experimental
Investigational medicinal product name	Novartis Meningococcal B Recombinant Vaccine
Investigational medicinal product code	V72
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5mL/1 dose

Arm title	B+R234

Arm description:

Subjects in this group received rMenB+OMV NZ vaccine at 2, 3, 4 months of age, administered concomitantly with routine infant vaccinations

Arm type	Experimental

Investigational medicinal product name	Novartis Meningococcal B Recombinant Vaccine
Investigational medicinal product code	V72
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:
0.5mL/1 dose

Arm title	R234

Arm description:
Subjects in this group received routine infant vaccines administered at 2, 3 and 4 months of age.

Arm type	Active comparator
Investigational medicinal product name	Infanrix Hexa and Prevenar
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:
0.5mL/1 dose

Number of subjects in period 1	B+R246	B246_R357	B+R234
Started	627	628	318
Completed	597	592	308
Not completed	30	36	10
Adverse event, serious fatal	4	7	2
Consent withdrawn by subject	12	15	3
Inappropriate enrollment	-	2	-
Lost to follow-up	7	9	3
Administrative reason	3	-	1
Protocol deviation	4	3	1

Number of subjects in period 1	R234
Started	312
Completed	302
Not completed	10
Adverse event, serious fatal	-
Consent withdrawn by subject	7
Inappropriate enrollment	-
Lost to follow-up	3
Administrative reason	-
Protocol deviation	-

Baseline characteristics

Reporting groups	
Reporting group title	B+R246
Reporting group description:	
Subjects in this group received rMenB+OMV NZ vaccine at 2, 4, and 6 months of age, administered concomitantly with routine infant vaccinations	
Reporting group title	B246_R357
Reporting group description:	
Subjects in this group received rMenB+OMV NZ vaccine at 2, 4, and 6 months of age; routine infant vaccinations were administered at 3, 5 and 7 months of age	
Reporting group title	B+R234
Reporting group description:	
Subjects in this group received rMenB+OMV NZ vaccine at 2, 3, 4 months of age, administered concomitantly with routine infant vaccinations	
Reporting group title	R234
Reporting group description:	
Subjects in this group received routine infant vaccines administered at 2, 3 and 4 months of age.	

Reporting group values	B+R246	B246_R357	B+R234
Number of subjects	627	628	318
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: days			
arithmetic mean	68.7	68.8	68.8
standard deviation	± 8.9	± 9.4	± 9.1
Gender categorical Units: Subjects			
Female	292	312	164
Male	335	316	154

Reporting group values	R234	Total	
Number of subjects	312	1885	
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: days			
arithmetic mean	68.1		
standard deviation	± 9	-	
Gender categorical			
Units: Subjects			
Female	159	927	
Male	153	958	

End points

End points reporting groups

Reporting group title	B+R246
Reporting group description:	
Subjects in this group received rMenB+OMV NZ vaccine at 2, 4, and 6 months of age, administered concomitantly with routine infant vaccinations	
Reporting group title	B246_R357
Reporting group description:	
Subjects in this group received rMenB+OMV NZ vaccine at 2, 4, and 6 months of age; routine infant vaccinations were administered at 3, 5 and 7 months of age	
Reporting group title	B+R234
Reporting group description:	
Subjects in this group received rMenB+OMV NZ vaccine at 2, 3, 4 months of age, administered concomitantly with routine infant vaccinations	
Reporting group title	R234
Reporting group description:	
Subjects in this group received routine infant vaccines administered at 2, 3 and 4 months of age.	

Primary: 1. Percentage of Subjects With Serum Bactericidal Activity ≥ 1:5

End point title	1. Percentage of Subjects With Serum Bactericidal Activity ≥ 1:5[1]
End point description:	
The percentage of subjects with serum bactericidal activity(hSBA)titer ≥1:5 after receiving three doses of rMenB+OMV NZ vaccine were evaluated to demonstrate sufficient immune response following rMenB+OMV NZ vaccination, when given concomitantly with routine infant vaccines to healthy infants The serum bactericidal antibodies directed against serogroup B meningococci, are measured by human complement Serum Bactericidal Assay (hSBA). The immune response was considered sufficient for groups B+R246 and B+R234 if the lower limit of the 2-sided 95% confidence interval was ≥ 70% for all three strains. The analysis was conducted on the MIIT population.	
End point type	Primary
End point timeframe:	
One month after third Men B 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: No statistical analysis is associated to this endpoint. Analyses were run descriptively.

End point values	B+R246	B246_R357	B+R234	R234
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	582	583	298	292
Units: Percentages of Participants				
number (confidence interval 95%)				
Baseline (5/99 strain; N=580,577,294,289)	5 (4 to 8)	7 (5 to 9)	5 (3 to 8)	6 (3 to 9)
Postvacc. (5/99 strain; N=551,554,285,245)	99 (98 to 100)	99 (98 to 100)	100 (99 to 100)	5 (3 to 8)
Baseline (NZ98/254 strain; N=582,583,298,292)	3 (2 to 5)	1 (0 to 2)	2 (1 to 4)	1 (0.083 to 2)
Postvacc. (NZ98/254 strain; N=555,559,284,269)	79 (75 to 82)	87 (84 to 89)	81 (76 to 85)	4 (2 to 8)
Postvacc. (44/76-SL strain;N=550,561,283,265)	9 (6 to 11)	7 (5 to 9)	6 (4 to 10)	6 (4 to 10)

Baseline (44/76-SL strain; N= 587,589,300,291)	99 (98 to 100)	99 (98 to 100)	99 (97 to 100)	4 (2 to 7)

Statistical analyses

No statistical analyses for this end point

Primary: 2. Safety and Tolerability of 3 Doses of rMenB

End point title	2. Safety and Tolerability of 3 Doses of rMenB[2]

End point description:

Safety and Tolerability of 3 Doses of rMenB was assessed in terms of the number of subjects who reported solicited local and systemic adverse events when administered concomitantly with routine infant vaccines at 2,4,6 months of age (B+R246) to when rMenB+OMV NZ and routine vaccines were administered separately (group B246_R357). Analysis was done on safety population.

End point type	Primary

End point timeframe:

10 months (groups 1 and 2); 8 months (groups 3 and 4)

Notes:

[2] - 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: No statistical analysis is associated to this endpoint. Analyses were run descriptively.

End point values	B+R246	B246_R357	B+R234	R234
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	624	627	318	311
Units: Participants				
Tenderness	529	491	265	0
Erythema	506	516	257	0
Induration	447	465	230	0
Swelling	290	324	149	0
Change Eat. Habits (N=624,626,318,311)	470	473	249	159
Sleepiness (N=624,626,318,311)	523	525	282	224
Vomiting (N=624,626,318,310)	193	234	97	83
Diarrhea (N=624,626,318,311)	284	327	138	113
Irritability (N=624,626,318,311)	543	527	289	220
Unusual Crying	526	515	268	186
Rash (N=624,626,318,311)	84	130	42	39
Fever (≥ 38.0C; N=624,627,318,311)	501	447	243	160

Statistical analyses

No statistical analyses for this end point

Secondary: 3. Non-inferiority of Immune Response to rMenB+OMV NZ Vaccination

End point title	3. Non-inferiority of Immune Response to rMenB+OMV NZ Vaccination[3]

End point description:

The non-inferiority of immune response to rMenB+OMV NZ vaccination when administered concomitantly with routine infant vaccines at 2,4,6 months of age (B+R246) to when rMenB+OMV NZ and routine vaccines were administered separately (group B246_R357) was assessed in terms of percentage of subjects With hSBA ≥ 1:5. Analysis was done on Per Protocol (PP) population.

End point type	Secondary

End point timeframe:

One month after 3rd Men B 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: No statistical analysis is associated to this endpoint. Analyses were run descriptively.

End point values	B+R246	B246_R357		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	556	548		
Units: Percentage of Participants				
number (confidence interval 95%)				
Baseline(44/76-SL strain)	8 (6 to 11)	7 (5 to 9)		
1 month post 3rd vacc.(44/76-SL; N=525,534)	100 (99 to 100)	100 (99 to 100)		
Baseline(5/99 strain; N=551,537)	6 (4 to 8)	7 (5 to 9)		
1 month post 3rd vacc.(5/99strain; N=527,529)	100 (99 to 100)	99 (98 to 100)		
Baseline(NZ98/254 strain; N=554,543)	3 (2 to 5)	1 (0 to 2)		
1 month post 3rdvacc.(NZ98/254; N=530,534)	79 (76 to 83)	87 (84 to 90)		

Statistical analyses

Statistical analysis title	Non-inferiority of immune responses against H44/76

Statistical analysis description:

Non-inferiority of immune responses against H44/76-SL strain when rMenB+OMV NZ vaccine was administered concomitantly with routine infant vaccines as compared to when rMenB+OMV NZ vaccine and routine vaccines were given separately

Comparison groups	B246_R357 v B+R246
Number of subjects included in analysis	1104
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Method	Miettinen and Nurminen method
Parameter estimate	Difference % (B+R246 minusB246_R357
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	1
Variability estimate	Standard deviation

Notes:

[4] - Immune response of Group B+R246 was considered non-inferior to response of Group B246_R357, if at one month after the third rMenB+OMV NZ injection the 2-sided 95% lower confidence limit of the difference in the percentage of subjects with hSBA titer ≥5 was greater than -10% for each of the 3 strains.

Statistical analysis title	Non-inferiority of immune responses against 5/99

Statistical analysis description:

Non-inferiority of immune responses against 5/99 strain when rMenB+OMV NZ vaccine was administered concomitantly with routine infant vaccines as compared to when rMenB+OMV NZ vaccine and routine vaccines were given separately.

Comparison groups	B+R246 v B246_R357
Number of subjects included in analysis	1104
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
Method	Miettinen and Nurminen method
Parameter estimate	Difference % (B+R246 minusB246_R357
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	1
Variability estimate	Standard deviation

Notes:

[5] - Immune response of Group B+R246 was considered non-inferior to response of Group B246_R357, if at one month after the third rMenB+OMV NZ injection the 2-sided 95% lower confidence limit of the difference in the percentage of subjects with hSBA titer ≥5 was greater than -10% for each of the 3 strains.

Statistical analysis title	Non-inferiority of immune responses -NZ98/254

Statistical analysis description:

Non-inferiority of immune responses against NZ98/254 strain when rMenB+OMV NZ vaccine was administered concomitantly with routine infant vaccines as compared to when rMenB+OMV NZ vaccine and routine vaccines were given separately

Comparison groups	B+R246 v B246_R357
Number of subjects included in analysis	1104
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
Method	Miettinen and Nurminen method
Parameter estimate	Difference % (B+R246 minusB246_R357
Point estimate	-8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12
upper limit	-4
Variability estimate	Standard deviation

Notes:

[6] - Immune response of Group B+R246 was considered non-inferior to response of Group B246_R357, if at one month after the third rMenB+OMV NZ injection the 2-sided 95% lower confidence limit of the difference in the percentage of subjects with hSBA titer ≥5 was greater than -10% for each of the 3 strains.

Secondary: 4. Non-inferiority of Immune Response to Diptheria and Tetanus Antigens

End point title	4. Non-inferiority of Immune Response to Diptheria and Tetanus Antigens[7]

End point description:

Non-inferiority of immune response to routine vaccine antigens when routine vaccines were administered concomitantly with rMenB+OMV NZ vaccine [group B+R234] to when only routine vaccines were given [Group R234] were assessed in terms of percentage of subjects with antibody concentrations ≥1.0 IU/mL against Diphtheria and Tetanus antigens as measured by enzyme-linked immunosorbent assay. Analysis was done on PP population.

End point type	Secondary

End point timeframe:

1 month after 3rd vaccination

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: No statistical analysis is associated to this endpoint. Analyses were run descriptively.

End point values	B+R234	R234		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	269	259		
Units: Percentage of Participants				
number (confidence interval 95%)				
Baseline (Diptheria)	25 (20 to 30)	21 (16 to 26)		
1 month after 3rd vacc. (Diptheria; N=261,232)	100 (99 to 100)	100 (98 to 100)		
Baseline (Tetanus)	81 (76 to 86)	86 (81 to 90)		
1 month after 3rd vacc. (Tetanus; N=261,232)	100 (99 to 100)	100 (98 to 100)		

Statistical analyses

Statistical analysis title	Non-inferiority -immune response against Diptheria

Statistical analysis description:

Non-inferiority of immune responses against Diptheria antigen when routine vaccine was administered concomitantly with rMenB+OMV NZ vaccine to when only routine vaccines were administered

Comparison groups	B+R234 v R234
Number of subjects included in analysis	528
Analysis specification	Pre-specified
Analysis type	non-inferiority[8]
Method	Miettinen and Nurminen method
Parameter estimate	Difference % (B+R234 minus R234)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	2
Variability estimate	Standard deviation

Notes:

[8] - Immune response of Group B+R234 was considered non-inferior to response of Group R234, if at one month after the third injection the 2-sided 95% lower confidence limit for the difference in the percentage of subjects with antibody response greater than the pre-specified cut off of for diphtheria (≥0.1 IU/mL) was >-10%.

Statistical analysis title	Non-inferiority- immune response against Tetanus

Statistical analysis description:

Non-inferiority of immune responses against Tetanus antigen when routine vaccine was administered concomitantly with rMenB+OMV NZ vaccine to when only routine vaccines were administered

Comparison groups	B+R234 v R234
Number of subjects included in analysis	528
Analysis specification	Pre-specified
Analysis type	non-inferiority[9]
Method	Miettinen and Nurminen method
Parameter estimate	Difference % (B+R234 minus R234)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	2
Variability estimate	Standard deviation

Notes:

[9] - Immune response of Group B+R234 was considered non-inferior to response of Group R234, if at one month after the third injection the 2-sided 95% lower confidence limit for the difference in the percentage of subjects with antibody response greater than the pre-specified cut off of for diphtheria (≥0.1 IU/mL) was >-10%.

Secondary: 5. Geometric Mean Titers Against Neisseria Meningitidis Serogroup B

End point title	5. Geometric Mean Titers Against Neisseria Meningitidis Serogroup B

End point description:

The hSBA antibody titers when rMenB+OMV NZ vaccine is administered concomitantly with routine infant vaccines to when rMenB+OMV NZ vaccine and routine vaccines were given separately are reported in terms of vaccine group- specific geometric mean titers. Analysis was done on PP population.

End point type	Secondary

End point timeframe:

One month after third Men B vaccination

End point values	B+R246	B246_R357	B+R234	R234
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	556	548	285	277
Units: Titres				
geometric mean (confidence interval 95%)				
Baseline (44/76-SL strain; N=556,548,285,277)	1.49 (1.4 to 1.59)	1.36 (1.28 to 1.46)	1.34 (1.23 to 1.46)	1.28 (1.19 to 1.37)
post vacc. (44/76-SL; N=525,534,273,253)	86 (80 to 92)	113 (105 to 121)	82 (75 to 91)	1.16 (1.09 to 1.24)
Baseline (5/99 strain; N=551,537,280,275)	1.3 (1.21 to 1.39)	1.28 (1.2 to 1.37)	1.19 (1.09 to 1.3)	1.24 (1.15 to 1.33)
post vacc. (5/99 strain; N=527,529,275,236)	537 (494 to 584)	699 (643 to 759)	325 (292 to 362)	1.25 (1.08 to 1.45)
Baseline (NZ98/254 strain; N=554,543,283,278)	1.13 (1.08 to 1.18)	1.08 (1.04 to 1.13)	1.06 (1 to 1.12)	1.07 (1.03 to 1.1)
post vacc. (NZ98/254strain; N=530,534,274,257)	12 (11 to 14)	18 (16 to 20)	11 (9.14 to 12)	1.11 (1.04 to 1.19)

Statistical analyses

No statistical analyses for this end point

Secondary: 6. Geometric Mean Ratio of hSBA Titers

End point title	6. Geometric Mean Ratio of hSBA Titers

End point description:

The geometric mean ratio (GMR) of GMTs at 1 month after 3rd rMenB+OMV NZ vaccination to prevaccination GMTs, when rMenB+OMV NZ was administered concomitantly with routine infant vaccines to when rMenB+OMV NZ vaccine and routine vaccines were given separately. Analysis was done on PP population.

End point type	Secondary

End point timeframe:

One month after third Men B vaccination versus baseline

End point values	B+R246	B246_R357	B+R234	R234
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	504	507	274	238
Units: Ratio				
number (confidence interval 95%)				
44/76-SL strain (N=501,507,262,236)	58 (52 to 64)	83 (74 to 92)	61 (53 to 70)	0.91 (0.83 to 1)
5/99 strain (N=497,494,257,217)	430 (379 to 487)	553 (489 to 625)	271 (231 to 318)	1.03 (0.86 to 1.22)
NZ98/254 strain (N=504,503,258,238)	11 (9.28 to 12)	16 (14 to 19)	10 (8.52 to 12)	1.05 (0.97 to 1.14)

Statistical analyses

No statistical analyses for this end point

Secondary: 7. Percentage of Subjects With hSBA ≥ 1:8

End point title	7. Percentage of Subjects With hSBA ≥ 1:8

End point description:

The percentage of subjects with hSBA titers ≥ 1:8, following rMenB+OMV NZ vaccination when given concomitantly with routine infant vaccines to when rMenB+OMV NZ and routine vaccines were given separately. Analysis was done on PP population.

End point type	Secondary

End point timeframe:

Percentage of Subjects With hSBA ≥ 1:8

End point values	B+R246	B246_R357	B+R234	R234
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	556	548	285	278
Units: Percentage of Participants				
number (confidence interval 95%)				
Baseline (44/76-SLstrain; N=556,548,285,277)	4 (3 to 6)	3 (2 to 5)	4 (2 to 7)	2 (1 to 5)
Post vacc. (44/76-SL; N=525,534,273,253)	99 (98 to 100)	100 (99 to 100)	99 (97 to 100)	2 (0 to 4)
Baseline (5/99strain; N=551,537,280,275)	4 (2 to 6)	3 (2 to 5)	2 (1 to 5)	4 (2 to 7)
Post vacc. (5/99strain; N=527,529,275,236)	100 (99 to 100)	99 (98 to 100)	100 (99 to 100)	3 (1 to 7)
Baseline(NZ98/254strain; N=554,543,283,278)	1 (1 to 3)	1 (0 to 2)	1 (0.086 to 3)	0.1 (0.0091 to 2)
Post vacc.(NZ98/254 strain; N=530,534,274,257)	67 (63 to 71)	79 (75 to 82)	69 (63 to 74)	2 (1 to 5)

Statistical analyses

No statistical analyses for this end point

Secondary: 8. Percentage of Subjects With 4-fold Rise in hSBA Titers

End point title	8. Percentage of Subjects With 4-fold Rise in hSBA Titers

End point description:

The percentage of subjects with 4-fold rise in hSBA titers at 1 month after 3rd rMenB+OMV NZ vaccination from baseline, when rMenB+OMV NZ was administered concomitantly with routine infant vaccines to when rMenB+OMV NZ vaccine and routine vaccines were given separately. Analysis was done on PP population.

End point type	Secondary

End point timeframe:

One month after third Men B vaccination

End point values	B+R246	B246_R357	B+R234	R234
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	501	507	262	238
Units: Percentage of Participants				
number (confidence interval 95%)				
44/76-SL strain (N=501,507,262,236)	97 (96 to 99)	99 (97 to 99)	98 (96 to 99)	1 (0 to 4)
5/99 strain (N=497,494,257,217)	99 (98 to 100)	99 (98 to 100)	100 (99 to 100)	3 (1 to 7)
NZ98/254 strain (N=504,503,258,238)	66 (62 to 70)	78 (74 to 81)	69 (63 to 75)	3 (1 to 5)

Statistical analyses

No statistical analyses for this end point

Secondary: 9. Non-inferiority of Immune Response to Acellular Pertussis Antigens

End point title	9. Non-inferiority of Immune Response to Acellular Pertussis Antigens[10]

End point description:

Non-inferiority of immune response to routine vaccine antigens when routine vaccines were administered concomitantly with rMenB+OMV NZ vaccine [group B+R234] to when only routine vaccines were given [Group R234] were assessed in terms of percentage of subjects achieving seroconversion for pertussis antigens -FHA, Pertactin and PT at 1 month after 3rd vaccination versus baseline
Seroconversion was defined as a 4-fold increase for each pertussis antigen or in those initially seropositive, persistence of the pre-vaccination antibody concentration at least at the same antibody concentration as before vaccination, taking into account the decay of maternal antibodies

End point type	Secondary

End point timeframe:

1 month after 3rd 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: No statistical analysis is associated to this endpoint. Analyses were run descriptively.

End point values	B+R234	R234		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239	210		
Units: Percentage of Participants				
number (confidence interval 95%)				
FHA	94 (90 to 97)	95 (91 to 97)		
Pertactin	92 (88 to 95)	95 (91 to 97)		
PT	97 (94 to 99)	98 (95 to 99)		

Statistical analyses

Statistical analysis title	Non-inferiority -immune response against Pertussis

Statistical analysis description:

Non-inferiority of immune responses against Pertussis antigen FHA when routine vaccine was administered concomitantly with rMenB+OMV NZ vaccine to when only routine vaccines were administered

Comparison groups	B+R234 v R234

Number of subjects included in analysis	449
Analysis specification	Pre-specified
Analysis type	non-inferiority[11]
Method	Miettinen and Nurminen method
Parameter estimate	Difference %(B+R234 minus R234)
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5
upper limit	4
Variability estimate	Standard deviation

Notes:

[11] - Group B+R234 was to be considered non-inferior to Group R234 if the 2-sided 95% lower confidence limit of this difference at 30 days after the last injection was greater than -10% for each of the antigens of the routine vaccinations

Statistical analysis title	Non-inferiority- immune response against Pertussis

Statistical analysis description:

Non-inferiority of immune responses against Pertussis antigen Pertactin when routine vaccine was administered concomitantly with rMenB+OMV NZ vaccine to when only routine vaccines were administered

Comparison groups	B+R234 v R234
Number of subjects included in analysis	449
Analysis specification	Pre-specified
Analysis type	non-inferiority[12]
Method	Miettinen and Nurminen method
Parameter estimate	Difference %(B+R234 minus R234)
Point estimate	-2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7
upper limit	2
Variability estimate	Standard deviation

Notes:

[12] - Group B+R234 was to be considered non-inferior to Group R234 if the 2-sided 95% lower confidence limit of this difference at 30 days after the last injection was greater than -10% for each of the antigens of the routine vaccinations

Statistical analysis title	Non-inferiority- immune response against Pertussis

Statistical analysis description:

Non-inferiority of immune responses against Pertussis antigen PT when routine vaccine was administered concomitantly with rMenB+OMV NZ vaccine to when only routine vaccines were administered

Comparison groups	B+R234 v R234
Number of subjects included in analysis	449
Analysis specification	Pre-specified
Analysis type	non-inferiority[13]
Method	Miettinen and Nurminen method
Parameter estimate	Difference %(B+R234 minus R234)
Point estimate	-1

Confidence interval	
level	95 %
sides	2-sided
lower limit	-4
upper limit	2
Variability estimate	Standard deviation

Notes:

[13] - Group B+R234 was to be considered non-inferior to Group R234 if the 2-sided 95% lower confidence limit of this difference at 30 days after the last injection was greater than -10% for each of the antigens of the routine vaccinations

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Throughout the study period	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups	
Reporting group title	B+R246
Reporting group description:	
Subjects in this group received rMenB+OMV NZ vaccine at 2, 4, and 6 months of age, administered concomitantly with routine infant vaccinations	
Reporting group title	B246_R357
Reporting group description:	
Subjects in this group received rMenB+OMV NZ vaccine at at 2, 4, and 6 months of age; routine infant vaccinations were administered at 3, 5 and 7 months of age	
Reporting group title	B+R234
Reporting group description:	
Subjects in this group received rMenB+OMV NZ vaccine at 2, 3, 4 months of age, administered concomitantly with routine infant vaccinations	
Reporting group title	R234
Reporting group description:	
Subjects in this group received routine infant vaccines administered at 2, 3 and 4 months of age.	

Serious adverse events	B+R246	B246_R357	B+R234
Total subjects affected by serious adverse events			
subjects affected / exposed	63 / 625 (10.08%)	57 / 627 (9.09%)	19 / 318 (5.97%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Glioma			
subjects affected / exposed	0 / 625 (0.00%)	0 / 627 (0.00%)	1 / 318 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemangioma			
subjects affected / exposed	0 / 625 (0.00%)	0 / 627 (0.00%)	1 / 318 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			

Kawasaki's disease			
subjects affected / exposed	1 / 625 (0.16%)	1 / 627 (0.16%)	0 / 318 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Prophylaxis			
subjects affected / exposed	0 / 625 (0.00%)	1 / 627 (0.16%)	0 / 318 (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
General disorders and administration site conditions			
Developmental delay			
subjects affected / exposed	1 / 625 (0.16%)	1 / 627 (0.16%)	0 / 318 (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
Hyperpyrexia			
subjects affected / exposed	1 / 625 (0.16%)	0 / 627 (0.00%)	0 / 318 (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
Pyrexia			
subjects affected / exposed	5 / 625 (0.80%)	4 / 627 (0.64%)	1 / 318 (0.31%)
occurrences causally related to treatment / all	4 / 5	2 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 625 (0.00%)	0 / 627 (0.00%)	0 / 318 (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
Hypersensitivity			
subjects affected / exposed	0 / 625 (0.00%)	0 / 627 (0.00%)	0 / 318 (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
Reproductive system and breast disorders			
Breast mass			

subjects affected / exposed	0 / 625 (0.00%)	1 / 627 (0.16%)	0 / 318 (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
Respiratory, thoracic and mediastinal disorders			
Apnoeic attack			
subjects affected / exposed	1 / 625 (0.16%)	0 / 627 (0.00%)	0 / 318 (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
Aspiration			
subjects affected / exposed	1 / 625 (0.16%)	0 / 627 (0.00%)	0 / 318 (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
Asthma			
subjects affected / exposed	1 / 625 (0.16%)	1 / 627 (0.16%)	0 / 318 (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
Wheezing			
subjects affected / exposed	1 / 625 (0.16%)	1 / 627 (0.16%)	0 / 318 (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
Psychiatric disorders			
Breath holding			
subjects affected / exposed	0 / 625 (0.00%)	1 / 627 (0.16%)	0 / 318 (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
Investigations			
Blood alkaline phosphatase abnormal			
subjects affected / exposed	1 / 625 (0.16%)	0 / 627 (0.00%)	0 / 318 (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
Body temperature increased			
subjects affected / exposed	1 / 625 (0.16%)	0 / 627 (0.00%)	0 / 318 (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

Injury, poisoning and procedural complications			
Exposure Via Ingestion			
subjects affected / exposed	1 / 625 (0.16%)	0 / 627 (0.00%)	0 / 318 (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
Burns second degree			
subjects affected / exposed	0 / 625 (0.00%)	0 / 627 (0.00%)	1 / 318 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	3 / 625 (0.48%)	0 / 627 (0.00%)	1 / 318 (0.31%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Exposure to toxic agent			
subjects affected / exposed	1 / 625 (0.16%)	0 / 627 (0.00%)	0 / 318 (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
Fall			
subjects affected / exposed	0 / 625 (0.00%)	2 / 627 (0.32%)	0 / 318 (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
Head injury			
subjects affected / exposed	0 / 625 (0.00%)	2 / 627 (0.32%)	0 / 318 (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
Joint dislocation			
subjects affected / exposed	0 / 625 (0.00%)	0 / 627 (0.00%)	1 / 318 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thermal burn			
subjects affected / exposed	0 / 625 (0.00%)	1 / 627 (0.16%)	0 / 318 (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

Craniocerebral Injury			
subjects affected / exposed	1 / 625 (0.16%)	0 / 627 (0.00%)	0 / 318 (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
Congenital, familial and genetic disorders			
Congenital musculoskeletal anomaly			
subjects affected / exposed	0 / 625 (0.00%)	0 / 627 (0.00%)	0 / 318 (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
Craniosynostosis			
subjects affected / exposed	0 / 625 (0.00%)	1 / 627 (0.16%)	0 / 318 (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
Cryptorchism			
subjects affected / exposed	1 / 625 (0.16%)	0 / 627 (0.00%)	0 / 318 (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
Talipes			
subjects affected / exposed	0 / 625 (0.00%)	1 / 627 (0.16%)	0 / 318 (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
Urachal abnormality			
subjects affected / exposed	0 / 625 (0.00%)	1 / 627 (0.16%)	0 / 318 (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
Nervous system disorders			
Convulsion			
subjects affected / exposed	0 / 625 (0.00%)	0 / 627 (0.00%)	1 / 318 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Crying			
subjects affected / exposed	1 / 625 (0.16%)	0 / 627 (0.00%)	0 / 318 (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

Epilepsy			
subjects affected / exposed	0 / 625 (0.00%)	2 / 627 (0.32%)	0 / 318 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile convulsion			
subjects affected / exposed	1 / 625 (0.16%)	2 / 627 (0.32%)	0 / 318 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotonia			
subjects affected / exposed	0 / 625 (0.00%)	1 / 627 (0.16%)	0 / 318 (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
Hypotonic hyporesponsive episode			
subjects affected / exposed	2 / 625 (0.32%)	0 / 627 (0.00%)	0 / 318 (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
Petit mal epilepsy			
subjects affected / exposed	0 / 625 (0.00%)	1 / 627 (0.16%)	0 / 318 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Lymphadentitis			
subjects affected / exposed	1 / 625 (0.16%)	0 / 627 (0.00%)	0 / 318 (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
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	0 / 625 (0.00%)	0 / 627 (0.00%)	1 / 318 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Retinal dystrophy			

subjects affected / exposed	0 / 625 (0.00%)	0 / 627 (0.00%)	1 / 318 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Strangulated hernia			
subjects affected / exposed	1 / 625 (0.16%)	0 / 627 (0.00%)	0 / 318 (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
Anal fistula			
subjects affected / exposed	1 / 625 (0.16%)	0 / 627 (0.00%)	0 / 318 (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
Diarrhoea			
subjects affected / exposed	1 / 625 (0.16%)	0 / 627 (0.00%)	0 / 318 (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
Enteritis			
subjects affected / exposed	0 / 625 (0.00%)	0 / 627 (0.00%)	0 / 318 (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
Gastritis			
subjects affected / exposed	0 / 625 (0.00%)	0 / 627 (0.00%)	0 / 318 (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
Gastrooesophageal reflux Disease			
subjects affected / exposed	1 / 625 (0.16%)	0 / 627 (0.00%)	0 / 318 (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
Inguinal hernia			
subjects affected / exposed	0 / 625 (0.00%)	1 / 627 (0.16%)	0 / 318 (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
Nausea			

subjects affected / exposed	0 / 625 (0.00%)	0 / 627 (0.00%)	1 / 318 (0.31%)
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	1 / 625 (0.16%)	1 / 627 (0.16%)	3 / 318 (0.94%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Purpura			
subjects affected / exposed	1 / 625 (0.16%)	0 / 627 (0.00%)	0 / 318 (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
Rash			
subjects affected / exposed	0 / 625 (0.00%)	1 / 627 (0.16%)	0 / 318 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Vesicoureteric reflux			
subjects affected / exposed	0 / 625 (0.00%)	1 / 627 (0.16%)	0 / 318 (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
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 625 (0.00%)	1 / 627 (0.16%)	0 / 318 (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
Synovitis			
subjects affected / exposed	0 / 625 (0.00%)	0 / 627 (0.00%)	1 / 318 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Bronchiolitis			

subjects affected / exposed	2 / 625 (0.32%)	3 / 627 (0.48%)	2 / 318 (0.63%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	4 / 625 (0.64%)	6 / 627 (0.96%)	2 / 318 (0.63%)
occurrences causally related to treatment / all	0 / 4	0 / 7	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
subjects affected / exposed	1 / 625 (0.16%)	4 / 627 (0.64%)	0 / 318 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Campylobacter gastroenteritis			
subjects affected / exposed	1 / 625 (0.16%)	0 / 627 (0.00%)	0 / 318 (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
Cellulitis			
subjects affected / exposed	0 / 625 (0.00%)	1 / 627 (0.16%)	0 / 318 (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
Enterovirus infection			
subjects affected / exposed	1 / 625 (0.16%)	0 / 627 (0.00%)	0 / 318 (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
Gastroenteritis			
subjects affected / exposed	7 / 625 (1.12%)	7 / 627 (1.12%)	2 / 318 (0.63%)
occurrences causally related to treatment / all	0 / 7	0 / 7	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis adenovirus			
subjects affected / exposed	0 / 625 (0.00%)	1 / 627 (0.16%)	0 / 318 (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 norovirus			

subjects affected / exposed	0 / 625 (0.00%)	1 / 627 (0.16%)	0 / 318 (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 rotavirus			
subjects affected / exposed	1 / 625 (0.16%)	1 / 627 (0.16%)	0 / 318 (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 / 625 (0.00%)	1 / 627 (0.16%)	0 / 318 (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
H1N1 influenza			
subjects affected / exposed	1 / 625 (0.16%)	0 / 627 (0.00%)	0 / 318 (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
Hand-foot-and mouth Disease			
subjects affected / exposed	0 / 625 (0.00%)	1 / 627 (0.16%)	0 / 318 (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
Influenza			
subjects affected / exposed	0 / 625 (0.00%)	1 / 627 (0.16%)	0 / 318 (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	0 / 625 (0.00%)	1 / 627 (0.16%)	1 / 318 (0.31%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	2 / 625 (0.32%)	1 / 627 (0.16%)	1 / 318 (0.31%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower respiratory tract infection viral			

subjects affected / exposed	1 / 625 (0.16%)	1 / 627 (0.16%)	0 / 318 (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
Lymph gland infection			
subjects affected / exposed	1 / 625 (0.16%)	0 / 627 (0.00%)	0 / 318 (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
Meningitis viral			
subjects affected / exposed	0 / 625 (0.00%)	1 / 627 (0.16%)	0 / 318 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasopharyngitis			
subjects affected / exposed	1 / 625 (0.16%)	1 / 627 (0.16%)	1 / 318 (0.31%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			
subjects affected / exposed	1 / 625 (0.16%)	1 / 627 (0.16%)	1 / 318 (0.31%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	2 / 625 (0.32%)	2 / 627 (0.32%)	0 / 318 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia respiratory syncytial viral			
subjects affected / exposed	0 / 625 (0.00%)	1 / 627 (0.16%)	0 / 318 (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
Pyelonephritis			
subjects affected / exposed	3 / 625 (0.48%)	0 / 627 (0.00%)	0 / 318 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			

subjects affected / exposed	0 / 625 (0.00%)	1 / 627 (0.16%)	0 / 318 (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
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	0 / 625 (0.00%)	1 / 627 (0.16%)	1 / 318 (0.31%)
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 syncytial virus infection			
subjects affected / exposed	1 / 625 (0.16%)	0 / 627 (0.00%)	0 / 318 (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
Rhinitis			
subjects affected / exposed	0 / 625 (0.00%)	1 / 627 (0.16%)	0 / 318 (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
Sepsis			
subjects affected / exposed	1 / 625 (0.16%)	1 / 627 (0.16%)	1 / 318 (0.31%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 625 (0.16%)	0 / 627 (0.00%)	0 / 318 (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
Tonsillitis			
subjects affected / exposed	0 / 625 (0.00%)	2 / 627 (0.32%)	0 / 318 (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
Upper respiratory tract infection			
subjects affected / exposed	1 / 625 (0.16%)	1 / 627 (0.16%)	1 / 318 (0.31%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			

subjects affected / exposed	3 / 625 (0.48%)	0 / 627 (0.00%)	0 / 318 (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
Varicella			
subjects affected / exposed	1 / 625 (0.16%)	0 / 627 (0.00%)	0 / 318 (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
Viral infection			
subjects affected / exposed	4 / 625 (0.64%)	1 / 627 (0.16%)	0 / 318 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	2 / 625 (0.32%)	0 / 627 (0.00%)	0 / 318 (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

Serious adverse events	R234		
Total subjects affected by serious adverse events			
subjects affected / exposed	19 / 312 (6.09%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Glioma			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemangioma			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Kawasaki's disease			

subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Prophylaxis			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Developmental delay			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyperpyrexia			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	1 / 312 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 312 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypersensitivity			
subjects affected / exposed	1 / 312 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Breast mass			

subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Apnoeic attack			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aspiration			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Asthma			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Wheezing			
subjects affected / exposed	1 / 312 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Breath holding			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Blood alkaline phosphatase abnormal			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Body temperature increased			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Injury, poisoning and procedural complications			
Exposure Via Ingestion			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Burns second degree			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Concussion			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Exposure to toxic agent			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fall			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Head injury			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Joint dislocation			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thermal burn			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Craniocerebral Injury				
subjects affected / exposed	0 / 312 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Congenital, familial and genetic disorders				
Congenital musculoskeletal anomaly				
subjects affected / exposed	1 / 312 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Craniosynostosis				
subjects affected / exposed	0 / 312 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cryptorchism				
subjects affected / exposed	0 / 312 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Talipes				
subjects affected / exposed	0 / 312 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urachal abnormality				
subjects affected / exposed	0 / 312 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Convulsion				
subjects affected / exposed	0 / 312 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Crying				
subjects affected / exposed	0 / 312 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Epilepsy			
subjects affected / exposed	1 / 312 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Febrile convulsion			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypotonia			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypotonic hyporesponsive episode			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Petit mal epilepsy			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Lymphadentitis			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Retinal dystrophy			

subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Strangulated hernia			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Anal fistula			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Enteritis			
subjects affected / exposed	1 / 312 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastritis			
subjects affected / exposed	1 / 312 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrooesophageal reflux Disease			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nausea			

subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Purpura			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rash			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Vesicoureteric reflux			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Synovitis			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchiolitis			

subjects affected / exposed	3 / 312 (0.96%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	2 / 312 (0.64%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Bronchopneumonia				
subjects affected / exposed	1 / 312 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Campylobacter gastroenteritis				
subjects affected / exposed	0 / 312 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	0 / 312 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enterovirus infection				
subjects affected / exposed	0 / 312 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	4 / 312 (1.28%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis adenovirus				
subjects affected / exposed	0 / 312 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis norovirus				

subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis rotavirus			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis salmonella			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
H1N1 influenza			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hand-foot-and mouth Disease			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Influenza			
subjects affected / exposed	1 / 312 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Laryngitis			
subjects affected / exposed	0 / 312 (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 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lower respiratory tract infection viral			

subjects affected / exposed	0 / 312 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lymph gland infection				
subjects affected / exposed	0 / 312 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meningitis viral				
subjects affected / exposed	0 / 312 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nasopharyngitis				
subjects affected / exposed	0 / 312 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Otitis media				
subjects affected / exposed	0 / 312 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	0 / 312 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia respiratory syncytial viral				
subjects affected / exposed	0 / 312 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	0 / 312 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis acute				

subjects affected / exposed	0 / 312 (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	1 / 312 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rhinitis			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Staphylococcal bacteraemia			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tonsillitis			
subjects affected / exposed	0 / 312 (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 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			

subjects affected / exposed	1 / 312 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Varicella			
subjects affected / exposed	0 / 312 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Viral infection			
subjects affected / exposed	1 / 312 (0.32%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 312 (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+R246	B246_R357	B+R234
Total subjects affected by non-serious adverse events			
subjects affected / exposed	620 / 625 (99.20%)	623 / 627 (99.36%)	316 / 318 (99.37%)
Nervous system disorders			
Somnolence			
subjects affected / exposed	523 / 625 (83.68%)	525 / 627 (83.73%)	282 / 318 (88.68%)
occurrences (all)	1229	1846	681
General disorders and administration site conditions			
Injection site induration			
subjects affected / exposed	489 / 625 (78.24%)	519 / 627 (82.78%)	254 / 318 (79.87%)
occurrences (all)	2553	2741	1357
Pyrexia			
subjects affected / exposed	514 / 625 (82.24%)	462 / 627 (73.68%)	246 / 318 (77.36%)
occurrences (all)	1294	1471	590
Injection site erythema			

subjects affected / exposed	535 / 625 (85.60%)	553 / 627 (88.20%)	271 / 318 (85.22%)
occurrences (all)	3395	3462	1787
Injection site swelling			
subjects affected / exposed	328 / 625 (52.48%)	383 / 627 (61.08%)	170 / 318 (53.46%)
occurrences (all)	1276	1307	697
Crying			
subjects affected / exposed	526 / 625 (84.16%)	516 / 627 (82.30%)	268 / 318 (84.28%)
occurrences (all)	1303	1781	674
Injection Site Pain			
subjects affected / exposed	544 / 625 (87.04%)	536 / 627 (85.49%)	279 / 318 (87.74%)
occurrences (all)	3087	2552	1624
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	302 / 625 (48.32%)	338 / 627 (53.91%)	145 / 318 (45.60%)
occurrences (all)	519	798	263
Teething			
subjects affected / exposed	30 / 625 (4.80%)	51 / 627 (8.13%)	7 / 318 (2.20%)
occurrences (all)	33	62	7
Vomiting			
subjects affected / exposed	208 / 625 (33.28%)	245 / 627 (39.07%)	100 / 318 (31.45%)
occurrences (all)	356	461	169
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	51 / 625 (8.16%)	96 / 627 (15.31%)	35 / 318 (11.01%)
occurrences (all)	62	121	43
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	100 / 625 (16.00%)	142 / 627 (22.65%)	50 / 318 (15.72%)
occurrences (all)	136	228	64
Eczema			
subjects affected / exposed	29 / 625 (4.64%)	35 / 627 (5.58%)	12 / 318 (3.77%)
occurrences (all)	34	41	15
Psychiatric disorders			
Irritability			
subjects affected / exposed	543 / 625 (86.88%)	527 / 627 (84.05%)	289 / 318 (90.88%)
occurrences (all)	1486	2326	775

Eating disorder			
subjects affected / exposed	470 / 625 (75.20%)	473 / 627 (75.44%)	249 / 318 (78.30%)
occurrences (all)	1035	1444	548
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	78 / 625 (12.48%)	98 / 627 (15.63%)	29 / 318 (9.12%)
occurrences (all)	113	126	33
Rhinitis			
subjects affected / exposed	67 / 625 (10.72%)	91 / 627 (14.51%)	28 / 318 (8.81%)
occurrences (all)	77	121	36
Bronchitis			
subjects affected / exposed	72 / 625 (11.52%)	82 / 627 (13.08%)	31 / 318 (9.75%)
occurrences (all)	107	113	40
Upper respiratory tract infection			
subjects affected / exposed	76 / 625 (12.16%)	72 / 627 (11.48%)	24 / 318 (7.55%)
occurrences (all)	100	108	32
Conjunctivitis			
subjects affected / exposed	53 / 625 (8.48%)	72 / 627 (11.48%)	26 / 318 (8.18%)
occurrences (all)	63	84	34
Viral infection			
subjects affected / exposed	42 / 625 (6.72%)	53 / 627 (8.45%)	17 / 318 (5.35%)
occurrences (all)	49	64	19
Ear infection			
subjects affected / exposed	48 / 625 (7.68%)	52 / 627 (8.29%)	15 / 318 (4.72%)
occurrences (all)	62	69	19
Gastroenteritis			
subjects affected / exposed	40 / 625 (6.40%)	45 / 627 (7.18%)	11 / 318 (3.46%)
occurrences (all)	43	51	12

Non-serious adverse events	R234		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	305 / 312 (97.76%)		
Nervous system disorders			
Somnolence			
subjects affected / exposed	224 / 312 (71.79%)		
occurrences (all)	492		
General disorders and administration site conditions			

Injection site induration subjects affected / exposed occurrences (all)	204 / 312 (65.38%) 681		
Pyrexia subjects affected / exposed occurrences (all)	176 / 312 (56.41%) 344		
Injection site erythema subjects affected / exposed occurrences (all)	229 / 312 (73.40%) 924		
Injection site swelling subjects affected / exposed occurrences (all)	115 / 312 (36.86%) 305		
Crying subjects affected / exposed occurrences (all)	187 / 312 (59.94%) 400		
Injection Site Pain subjects affected / exposed occurrences (all)	182 / 312 (58.33%) 612		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	123 / 312 (39.42%) 243		
Teething subjects affected / exposed occurrences (all)	13 / 312 (4.17%) 13		
Vomiting subjects affected / exposed occurrences (all)	85 / 312 (27.24%) 145		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	41 / 312 (13.14%) 49		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	47 / 312 (15.06%) 66		

Eczema			
subjects affected / exposed	17 / 312 (5.45%)		
occurrences (all)	20		
Psychiatric disorders			
Irritability			
subjects affected / exposed	220 / 312 (70.51%)		
occurrences (all)	544		
Eating disorder			
subjects affected / exposed	159 / 312 (50.96%)		
occurrences (all)	316		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	35 / 312 (11.22%)		
occurrences (all)	51		
Rhinitis			
subjects affected / exposed	36 / 312 (11.54%)		
occurrences (all)	48		
Bronchitis			
subjects affected / exposed	23 / 312 (7.37%)		
occurrences (all)	30		
Upper respiratory tract infection			
subjects affected / exposed	16 / 312 (5.13%)		
occurrences (all)	24		
Conjunctivitis			
subjects affected / exposed	22 / 312 (7.05%)		
occurrences (all)	28		
Viral infection			
subjects affected / exposed	26 / 312 (8.33%)		
occurrences (all)	29		
Ear infection			
subjects affected / exposed	14 / 312 (4.49%)		
occurrences (all)	16		
Gastroenteritis			
subjects affected / exposed	12 / 312 (3.85%)		
occurrences (all)	13		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported