



Clinical trial results:

Safety and Immunogenicity of GSK Meningococcal Group B Vaccine and 13-valent Pneumococcal Vaccine administered concomitantly with Routine Infant Vaccines to Healthy Infants

Summary

EudraCT number	2016-003268-37
Trial protocol	Outside EU/EEA
Global end of trial date	27 December 2024

Results information

Result version number	v2 (current)
This version publication date	05 September 2026
First version publication date	13 March 2026
Version creation reason	• Correction of full data set Results have been amended to account for consistency with other registries.

Trial information

Trial identification

Sponsor protocol code	205239
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03621670
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	79 New Oxford Street, London, WC1A1DG, United Kingdom, TW8 9GS
Public contact	GSK Response Center, GlaxoSmithKline, 44 8664357343, GSKClinicalSupportHD@gsk.com
Scientific contact	GSK Response Center, GlaxoSmithKline, 44 8664357343, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	15 October 2025
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	27 December 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To assess the safety and tolerability of rMenB+OMV NZ, PCV13 and other RIV when administered concomitantly to healthy infants at 2, 4, 6 and 12 months of age, throughout the study duration.
- To demonstrate the sufficiency of the immune response to rMenB+OMV NZ when administered concomitantly with PCV13 and other RIV to healthy infants at 2, 4 and 6 months of age, at 1 month after the 3rd vaccination.
- To demonstrate the sufficiency of the immune response to rMenB+OMV NZ when administered concomitantly with PCV13 and other RIV to healthy infants at 2, 4, 6 and 12 months of age, at 1 month after the 4th vaccination.
- To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV to healthy infants 2, 4 and 6 months of age, compared to PCV13 without rMenB+OMV NZ, at 1 month after the 3rd vaccination.

Protection of trial subjects:

All subjects were observed closely for at least 30 minutes in the clinic after vaccination, with appropriate medical treatment readily available in case of a rare anaphylactic reaction following the administration of vaccines. Study vaccines were administered only by personnel qualified to perform that function according to the routine clinical practice and under applicable local laws and regulations for the specific study site. All subjects were followed up for safety for a period of 6 months to 1 year after the last vaccination.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 July 2018
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	United States: 1196
Worldwide total number of subjects	1196
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0

Infants and toddlers (28 days-23 months)	1196
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: -

Pre-assignment

Screening details:

Out of the 1196 participants enrolled, only 1184 participants were included in the Exposed Set and started the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	MenB+PCV Group

Arm description:

Infant participants received rMenB+OMV NZ (Bexsero) along with PCV13 (Prevnam 13), Pediarix, Hiberix and Rotarix on Day 1 and Day 61 followed by rMenB+OMV NZ, PCV13, Pediarix and Hiberix on Day 121 and rMenB+OMV NZ, PCV13/PCV20, M-M-R II and Varivax on Day 301.

Arm type	Experimental
Investigational medicinal product name	Bexsero
Investigational medicinal product code	
Other name	GSK Biologicals' Meningococcal group-B vaccine/ rMenB+OMV NZ
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

4 doses per participant

Investigational medicinal product name	Prevnam13/20
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

4 doses per participant

Investigational medicinal product name	Pediarix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses per participant

Investigational medicinal product name	Varivax
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:	
1 dose per participant	
Investigational medicinal product name	Rotarix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral liquid
Routes of administration	Oral use
Dosage and administration details:	
2 doses per participant	
Investigational medicinal product name	M-M-R II
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
1 dose per participant	
Investigational medicinal product name	Hiberix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
3 doses per participant	
Arm title	Placebo+PCV Group
Arm description:	
Infant participants received PCV13 along with placebo, Pediarix, Hiberix and Rotarix on Day 1 and Day 61 followed by PCV13, Placebo, Pediarix and Hiberix on Day 121 and PCV13/PCV20, Placebo M-M-R II and Varivax on Day 301.	
Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
4 doses per participant	
Investigational medicinal product name	Pediarix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use
Dosage and administration details:	
3 doses per participant	
Investigational medicinal product name	Varivax
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
1 dose per participant	

Investigational medicinal product name	Rotarix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral liquid
Routes of administration	Oral use
Dosage and administration details:	
2 doses per participant	
Investigational medicinal product name	M-M-R II
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details:	
1 dose per participant	
Investigational medicinal product name	Prevnar13/20
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in pre-filled syringe
Routes of administration	Intramuscular use
Dosage and administration details:	
4 doses per participant	
Investigational medicinal product name	Hiberix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
3 doses per participant	

Number of subjects in period 1^[1]	MenB+PCV Group	Placebo+PCV Group
Started	781	403
Completed	642	326
Not completed	139	77
Adverse event, non-fatal	3	1
Not willing / Not able to be contacted	9	13
Protocol Deviation	7	3
Not specified	13	5
Lost to follow-up	32	25
Consent withdrawal not due to AEs	54	18
Migrated / Moved from the study area	21	12

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Out of the 1196 participants enrolled, only 1184 participants were included in the Exposed Set and started the study.

Baseline characteristics

Reporting groups

Reporting group title	MenB+PCV Group
Reporting group description:	
Infant participants received rMenB+OMV NZ (Bexsero) along with PCV13 (Pevnar 13), Pediarix, Hiberix and Rotarix on Day 1 and Day 61 followed by rMenB+OMV NZ, PCV13, Pediarix and Hiberix on Day 121 and rMenB+OMV NZ, PCV13/PCV20, M-M-R II and Varivax on Day 301.	
Reporting group title	Placebo+PCV Group
Reporting group description:	
Infant participants received PCV13 along with placebo, Pediarix, Hiberix and Rotarix on Day 1 and Day 61 followed by PCV13, Placebo, Pediarix and Hiberix on Day 121 and PCV13/PCV20, Placebo M-M-R II and Varivax on Day 301.	

Reporting group values	MenB+PCV Group	Placebo+PCV Group	Total
Number of subjects	781	403	1184
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	781	403	1184
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Sex: Female, Male			
Units: Participants			
Male	401	207	608
Female	380	196	576
Race/Ethnicity, Customized			
Units: Subjects			
Asian	39	21	60
Black or African American	84	33	117
White	531	288	819
Other (Not specified)	107	56	163
American Indian or Alaska Native	17	4	21
Native Hawaiian or Other Pacific Islander	3	1	4

End points

End points reporting groups

Reporting group title	MenB+PCV Group
Reporting group description:	
Infant participants received rMenB+OMV NZ (Bexsero) along with PCV13 (Pevnar 13), Pediarix, Hiberix and Rotarix on Day 1 and Day 61 followed by rMenB+OMV NZ, PCV13, Pediarix and Hiberix on Day 121 and rMenB+OMV NZ, PCV13/PCV20, M-M-R II and Varivax on Day 301.	
Reporting group title	Placebo+PCV Group
Reporting group description:	
Infant participants received PCV13 along with placebo, Pediarix, Hiberix and Rotarix on Day 1 and Day 61 followed by PCV13, Placebo, Pediarix and Hiberix on Day 121 and PCV13/PCV20, Placebo M-M-R II and Varivax on Day 301.	

Primary: Number of participants reporting any solicited administration site events after the first vaccination administered at Day 1

End point title	Number of participants reporting any solicited administration site events after the first vaccination administered at Day 1 ^[1]
End point description:	
Assessed solicited administration site events include injection site tenderness (administration site pain), erythema (redness), swelling and induration. Any solicited administration site events = occurrence of the event regardless of intensity grade. Data for Rotarix is not presented as it was administered orally. Analysis was performed on the Solicited Safety Set, which included all participants who received a study vaccination and had solicited adverse event data available for the specified duration. Participants in the Placebo+PCV group did not receive Bexsero vaccine, hence they were not analyzed.	
End point type	Primary
End point timeframe:	
Day 1 to Day 7	

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: The analysis of this primary endpoint was descriptive i.e. No statistical hypothesis test was performed.

End point values	MenB+PCV Group	Placebo+PCV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	768	394		
Units: Participants				
Erythema, Bexsero	156	0		
Erythema, Pevnar 13	100	39		
Erythema, Placebo	0	25		
Erythema, Pediarix	72	32		
Erythema, Hiberix	74	17		
Induration, Bexsero	204	0		
Induration, Pevnar 13	127	67		
Induration, Placebo	0	22		
Induration, Pediarix	70	34		
Induration, Hiberix	77	20		
Swelling, Bexsero	132	0		
Swelling, Pevnar 13	77	34		
Swelling, Placebo	0	21		
Swelling, Pediarix	53	21		

Swelling, Hiberix	54	12		
Tenderness, Bexsero	352	0		
Tenderness, Prevna 13	310	107		
Tenderness, Placebo	0	81		
Tenderness, Pediarix	270	92		
Tenderness, Hiberix	284	74		

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants reporting any solicited systemic events after the first vaccination administered at Day 1

End point title	Number of participants reporting any solicited systemic events after the first vaccination administered at Day 1 ^[2]
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End point description:

Assessed systemic events include change in eating habits, sleepiness, vomiting, diarrhea, irritability, persistent crying, and fever, defined as body temperature greater than or equal to ($\geq$)38.0°C/100.4°F. Any solicited systemic events = occurrence of the event regardless of intensity grade. Analysis was performed on the Solicited Safety Set. Only participants with data available at the specified timepoints were included in this analysis.

End point type	Primary
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End point timeframe:

Day 1 to Day 7

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: The analysis of this primary endpoint was descriptive i.e. No statistical hypothesis test was performed.

End point values	MenB+PCV Group	Placebo+PCV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	768	394		
Units: Participants				
Change in eating habits	329	122		
Diarrhea	173	84		
Irritability	601	242		
Persistent crying	248	89		
Sleepiness	560	246		
Vomiting	176	79		
Fever	252	34		

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants reporting any solicited administration site events after the second vaccination administered at Day 61

End point title	Number of participants reporting any solicited administration
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End point description:

Data for Rotarix is not presented as it was administered orally. Analysis was performed on the Solicited Safety Set. Only participants with data available at the specified timepoints were included in this analysis.

End point type	Primary
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End point timeframe:

Day 61 to Day 67

Notes:

[3] - 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: The analysis of this primary endpoint was descriptive i.e. No statistical hypothesis test was performed.

End point values	MenB+PCV Group	Placebo+PCV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	699	364		
Units: Participants				
Erythema, Bexsero	200	0		
Erythema, Prevnar 13	129	62		
Erythema, Placebo	0	44		
Erythema, Pediarix	99	54		
Erythema, Hiberix	86	41		
Induration, Bexsero	213	0		
Induration, Prevnar 13	142	63		
Induration, Placebo	0	32		
Induration, Pediarix	109	55		
Induration, Hiberix	80	32		
Swelling, Bexsero	112	0		
Swelling, Prevnar 13	74	38		
Swelling, Placebo	0	19		
Swelling, Pediarix	52	33		
Tenderness, Bexsero	269	0		
Swelling, Hiberix	49	17		
Tenderness, Prevnar 13	227	81		
Tenderness, Placebo	0	65		
Tenderness, Pediarix	201	67		
Tenderness, Hiberix	207	52		

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants reporting any solicited systemic events after the second vaccination administered at Day 61

End point title	Number of participants reporting any solicited systemic events after the second vaccination administered at Day 61 ^[4]
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End point description:

Analysis was performed on the Solicited Safety Set. Only participants with data available at the specified timepoints were included in this analysis.

End point type	Primary
End point timeframe:	
Day 61 to Day 67	
Notes:	
[4] - 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: The analysis of this primary endpoint was descriptive i.e. No statistical hypothesis test was performed.	

End point values	MenB+PCV Group	Placebo+PCV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	699	364		
Units: Participants				
Change in eating habits	238	90		
Diarrhea	119	66		
Irritability	514	215		
Persistent crying	209	73		
Sleepiness	455	183		
Vomiting	104	49		
Fever	269	64		

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants reporting any solicited administration site events after the third vaccination administered at Day 121

End point title	Number of participants reporting any solicited administration site events after the third vaccination administered at Day 121 ^[5]
End point description:	
Analysis was performed on the Solicited Safety Set. Only participants with data available at the specified timepoints were included in this analysis. Participants in the Placebo+PCV group did not receive Bexsero vaccine, hence they were not analyzed.	
End point type	Primary
End point timeframe:	
Day 121 to Day 127	
Notes:	
[5] - 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: The analysis of this primary endpoint was descriptive i.e. No statistical hypothesis test was performed.	

End point values	MenB+PCV Group	Placebo+PCV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	676	352		
Units: Participants				
Erythema, Bexsero	181	0		
Erythema, Prevnar 13	127	71		
Erythema, Placebo	0	43		
Erythema, Pediarix	114	65		

Erythema, Hiberix	97	38		
Induration, Bexsero	187	0		
Induration, Prevnar 13	128	60		
Induration, Placebo	0	26		
Induration, Pediarix	124	70		
Induration, Hiberix	86	28		
Swelling, Bexsero	103	0		
Swelling, Prevnar 13	67	39		
Swelling, Placebo	0	13		
Swelling, Pediarix	55	28		
Swelling, Hiberix	36	8		
Tenderness, Bexsero	244	0		
Tenderness, Prevnar 13	210	66		
Tenderness, Placebo	0	52		
Tenderness, Pediarix	188	58		
Tenderness, Hiberix	194	45		

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants reporting any solicited systemic events after the third vaccination administered at Day 121

End point title	Number of participants reporting any solicited systemic events after the third vaccination administered at Day 121 ^[6]
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End point description:

Analysis was performed on the Solicited Safety Set. Only participants with data available at the specified timepoints were included in this analysis.

End point type	Primary
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End point timeframe:

Day 121 to Day 127

Notes:

[6] - 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: The analysis of this primary endpoint was descriptive i.e. No statistical hypothesis test was performed.

End point values	MenB+PCV Group	Placebo+PCV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	676	352		
Units: Participants				
Change in eating habits	205	94		
Diarrhea	87	44		
Irritability	454	179		
Persistent crying	151	59		
Sleepiness	326	142		
Vomiting	88	46		
Fever	216	55		

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants reporting any solicited administration site events after the fourth vaccination administered at Day 301

End point title	Number of participants reporting any solicited administration site events after the fourth vaccination administered at Day 301 ^[7]
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End point description:

Analysis was performed on the Solicited Safety Set. Only participants with data available at the specified timepoints were included in this analysis.

End point type	Primary
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End point timeframe:

Day 301 to Day 307

Notes:

[7] - 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: The analysis of this primary endpoint was descriptive i.e. No statistical hypothesis test was performed.

End point values	MenB+PCV Group	Placebo+PCV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	579	299		
Units: Participants				
Erythema, Bexsero	180	0		
Erythema, Prevnar 13/20	119	37		
Erythema, Placebo	0	25		
Erythema, MMR II	64	24		
Erythema, Varivax	62	20		
Induration, Bexsero	179	0		
Induration, Prevnar 13/20	109	32		
Induration, Placebo	0	24		
Induration, MMR II	46	17		
Induration, Varivax	38	15		
Swelling, Bexsero	91	0		
Swelling, Prevnar 13/20	52	18		
Swelling, Placebo	0	8		
Swelling, MMR II	26	12		
Swelling, Varivax	23	9		
Tenderness, Bexsero	223	0		
Tenderness, Prevnar 13/20	181	35		
Tenderness, Placebo	0	31		
Tenderness, MMR II	130	28		
Tenderness, Varivax	119	27		

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants reporting any solicited systemic events after the fourth vaccination administered at Day 301

End point title	Number of participants reporting any solicited systemic events after the fourth vaccination administered at Day 301 ^[8]
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End point description:

Analysis was performed on the Solicited Safety Set. Only participants with data available at the specified timepoints were included in this analysis.

End point type	Primary
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End point timeframe:

Day 301 to Day 307

Notes:

[8] - 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: The analysis of this primary endpoint was descriptive i.e. No statistical hypothesis test was performed.

End point values	MenB+PCV Group	Placebo+PCV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	614	314		
Units: Participants				
Change in eating habits	219	75		
Diarrhea	85	40		
Irritability	401	153		
Persistent crying	115	29		
Rash	71	30		
Sleepiness	273	96		
Vomiting	60	32		
Fever	118	22		

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants with any solicited systemic AEs during the 30 days after the fourth vaccination at Day 301

End point title	Number of participants with any solicited systemic AEs during the 30 days after the fourth vaccination at Day 301 ^[9]
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End point description:

Systemic events assessed included rash, parotid/salivary gland swelling, and fever. These systemic adverse events were recorded for 30 days following MMR and VV vaccine administration. Any solicited systemic events = occurrence of the event regardless of intensity grade. Analysis was performed on the

Solicited Safety Set. Only participants with data available at the specified timepoints were included in this analysis.

End point type	Primary
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End point timeframe:

Day 301 to Day 330

Notes:

[9] - 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: The analysis of this primary endpoint was descriptive i.e. No statistical hypothesis test was performed.

End point values	MenB+PCV Group	Placebo+PCV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	627	321		
Units: Participants				
Parotid/Salivary gland swelling	20	17		
Rash	206	95		
Fever	197	70		

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants reporting any unsolicited adverse events (AEs) after the first vaccination administered at Day 1

End point title	Number of participants reporting any unsolicited adverse events (AEs) after the first vaccination administered at Day 1 ^[10]
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End point description:

An unsolicited AEs is an AE that is not solicited using a subject diary and that is spontaneously communicated by the parent(s)/ Legally Authorized Representatives (LARs) who has signed the informed consent or a solicited local or systemic AE that continues beyond the solicited period after vaccination. Any = occurrence of the event regardless of the intensity grade. Analysis was performed on the Unsolicited Safety Set, which included all participants who received a study vaccination and had unsolicited adverse event data available for the specified duration.

End point type	Primary
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End point timeframe:

Day 1 to Day 30

Notes:

[10] - 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: The analysis of this primary endpoint was descriptive i.e. No statistical hypothesis test was performed.

End point values	MenB+PCV Group	Placebo+PCV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	775	401		
Units: Participants	214	103		

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants reporting any SAEs, AEs leading to withdrawal, AESIs and MAAEs

End point title	Number of participants reporting any SAEs, AEs leading to withdrawal, AESIs and MAAEs ^[11]
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End point description:

An SAE is any untoward medical occurrence that results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization and that results in disability/incapacity. An AE leading to withdrawal includes any AEs/SAEs collected and recorded from the time of the 1st receipt of study vaccines until study end which are identified as reasons for withdrawal of the participant from the study. AESIs are pre-defined (serious or non-serious) AEs of scientific and medical concern specific to the product or program which might warrant further investigation in order to characterize and understand it. MAAEs includes any AEs that required hospitalization, or an otherwise unscheduled visit to or from medical personnel for any reason, including emergency room visits. Analysis was performed on the Unsolicited Safety Set. Only participants with data available at the specified timepoints were included in this analysis.

End point type	Primary
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End point timeframe:

Day 1 up to study end (Day 481 for participants who have not reached 6-month follow-up at the time of Protocol Amendment 7; Day 661 for all others)

Notes:

[11] - 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: The analysis of this primary endpoint was descriptive i.e. No statistical hypothesis test was performed.

End point values	MenB+PCV Group	Placebo+PCV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	775	401		
Units: Participants				
AEs leading to withdrawal	3	1		
SAEs	35	19		
AESIs	6	3		
MAAEs	626	329		

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants reporting any unsolicited AEs after the fourth vaccination administered at day 301

End point title	Number of participants reporting any unsolicited AEs after the fourth vaccination administered at day 301 ^[12]
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End point description:

Analysis was performed on the Unsolicited Safety Set. Only participants with data available at the specified timepoints were included in this analysis.

End point type	Primary
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End point timeframe:

Day 301 to Day 330

Notes:

[12] - 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: The analysis of this primary endpoint was descriptive i.e. No statistical hypothesis test was performed.

End point values	MenB+PCV Group	Placebo+PCV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	668	339		
Units: Participants	248	144		

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants reporting any unsolicited AEs after the third vaccination administered at Day 121

End point title	Number of participants reporting any unsolicited AEs after the third vaccination administered at Day 121 ^[13]
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End point description:

Analysis was performed on the Unsolicited Safety Set. Only participants with data available at the specified timepoints were included in this analysis.

End point type	Primary
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End point timeframe:

Day 121 to Day 150

Notes:

[13] - 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: The analysis of this primary endpoint was descriptive i.e. No statistical hypothesis test was performed.

End point values	MenB+PCV Group	Placebo+PCV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	725	374		
Units: Participants	230	120		

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants reporting any unsolicited AEs after the second vaccination administered at Day 61

End point title	Number of participants reporting any unsolicited AEs after the second vaccination administered at Day 61 ^[14]
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End point description:

Analysis was performed on the Unsolicited Safety Set. Only participants with data available at the specified timepoints were included in this analysis.

End point type	Primary
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End point timeframe:

Day 61 to Day 90

Notes:

[14] - 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: The analysis of this primary endpoint was descriptive i.e. No statistical hypothesis test was performed.

End point values	MenB+PCV Group	Placebo+PCV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	745	388		
Units: Participants	225	119		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with human serum bactericidal assay (hSBA) antibody titers $\geq$ Lower Limit of Quantitation (LLOQ) for each of the Serogroup B test strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4) and M13520 (NHBA)

End point title	Percentage of participants with human serum bactericidal assay (hSBA) antibody titers $\geq$ Lower Limit of Quantitation (LLOQ) for each of the Serogroup B test strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4) and M13520 (NHBA) ^{[15][16]}
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End point description:

Serum bactericidal activity is assessed using hSBA against *Neisseria meningitidis* serogroup B test strains: M14459 (fHbp); 96217 (NadA); NZ98/254 (PorA P1.4); M13520 (NHBA). The sufficiency of the immune response to rMenB+OMV NZ at one month after the third vaccination was to be demonstrated if the lower confidence limit for the percentage of participants achieving hSBA titers $\geq$ LLOQ is $\geq$ 60% for each of the M14459, 96217, NZ98/254, M13520 test strain. This outcome measure evaluated immune response to the rMenB+OMV NZ vaccine only, hence it was not applicable to the Placebo+PCV group. Analysis was performed on the Per Protocol Set (PPS) for immunogenicity, which included all participants in the Full Analysis Set (FAS) who correctly received the vaccine, with no protocol deviation and are not excluded due to other reasons defined prior to unblinding or analysis. Only participants with data available for the specified analysis at the specified timepoint were included.

End point type	Primary
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End point timeframe:

At Day 151 (1 month after the third vaccination)

Notes:

[15] - 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: The analysis of this primary endpoint was descriptive i.e. No statistical hypothesis test was performed.

[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: This outcome measure evaluated immune response to the rMenB+OMV NZ vaccine only, hence it was not applicable to the Placebo+PCV group.

End point values	MenB+PCV Group			
Subject group type	Reporting group			
Number of subjects analysed	553			
Units: Percentage of participants				
number (confidence interval 99.2%)				
M14459 (fHbp)	92.2 (88.6 to 94.9)			
96217 (NadA)	99.4 (97.9 to 99.9)			
NZ98/254 (PorA)	73.5 (68.2 to 78.3)			
M13520 (NHBA)	53.0 (47.3 to 58.6)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with hSBA titers $\geq$ LLOQ against all serogroup B test strains combined (composite response)

End point title	Percentage of participants with hSBA titers $\geq$ LLOQ against all serogroup B test strains combined (composite response) ^{[17][18]}
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End point description:

The immune response to the rMenB+OMV NZ vaccine is assessed by measuring serum bactericidal activity using hSBA against four *Neisseria meningitidis* serogroup B test strains: M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4), and M13520 (NHBA). The composite response is defined as the percentage of participants with hSBA titers $\geq$ Lower Limit of Quantitation (LLOQ) across all four strains combined. The sufficiency of the immune response to rMenB+OMV NZ at one month after the third vaccination was to be demonstrated if the lower confidence limit for the percentage of participants achieving hSBA titers $\geq$ LLOQ is $\geq$ 50% for all strains combined. This outcome measure evaluated immune response to the rMenB+OMV NZ vaccine only, hence it was not applicable to the Placebo+PCV group. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

End point type	Primary
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End point timeframe:

At Day 151 (1 month after the third vaccination)

Notes:

[17] - 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: The analysis of this primary endpoint was descriptive i.e. No statistical hypothesis test was performed.

[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: This outcome measure evaluated immune response to the rMenB+OMV NZ vaccine only, hence it was not applicable to the Placebo+PCV group.

End point values	MenB+PCV Group			
Subject group type	Reporting group			
Number of subjects analysed	524			
Units: Percentage of participants				
number (confidence interval 99.2%)	42.7 (37.0 to 48.6)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with hSBA Antibody Titers ≥ 8 for Strains M14459 (fHbp), NZ98/254 (PorA P1.4), and M13520 (NHBA) and ≥ 16 for Strain 96217 (NadA) (Composite response across all strains)

End point title	Percentage of Participants with hSBA Antibody Titers ≥ 8 for Strains M14459 (fHbp), NZ98/254 (PorA P1.4), and M13520 (NHBA) and ≥ 16 for Strain 96217 (NadA) (Composite response across all strains) ^{[19][20]}
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End point description:

The immune response to the rMenB+OMV NZ vaccine is assessed by measuring serum bactericidal activity using hSBA against four *Neisseria meningitidis* serogroup B test strains: M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4), and M13520 (NHBA). The composite response is defined as the percentage of participants with hSBA titers $\geq$ Lower Limit of Quantitation (LLOQ) across all four strains combined. The sufficiency of the immune response to rMenB+OMV NZ at one month after the 4th vaccination was to be demonstrated if the lower confidence limit for the percentage of participants achieving hSBA titers ≥ 8 (for strains M14459, NZ98/254, M13520) and ≥ 16 (for strain 96217) is $\geq 65\%$ for all strains combined. This outcome measure evaluated immune response to the rMenB+OMV NZ vaccine only, hence it was not applicable to the Placebo+PCV group. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

End point type	Primary
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End point timeframe:

At Day 331 (1 month after the fourth vaccination)

Notes:

[19] - 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: The analysis of this primary endpoint was descriptive i.e. No statistical hypothesis test was performed.

[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: This outcome measure evaluated immune response to the rMenB+OMV NZ vaccine only, hence it was not applicable to the Placebo+PCV group.

End point values	MenB+PCV Group			
Subject group type	Reporting group			
Number of subjects analysed	478			
Units: Percentage of participants				
number (confidence interval 95.8%)	63.2 (58.5 to 67.7)			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants with hSBA Antibody Titers ≥ 8 for Strains M14459 (fHbp); 96217 (NadA); NZ98/254 (PorA P1.4); M13520 (NHBA) and ≥ 16 for Strain 96217

End point title	Percentage of Participants with hSBA Antibody Titers ≥ 8 for Strains M14459 (fHbp); 96217 (NadA); NZ98/254 (PorA P1.4); M13520 (NHBA) and ≥ 16 for Strain 96217 ^[21] ^[22]
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End point description:

Serum bactericidal activity is assessed using human complement (hSBA) against *Neisseria meningitidis* serogroup B test strains: M14459 (fHbp); 96217 (NadA); NZ98/254 (PorA P1.4); M13520 (NHBA). The sufficiency of the immune response to rMenB+OMV NZ at one month after the 4th vaccination was to be demonstrated if the lower confidence limit for the percentage of participants achieving hSBA titers ≥ 8 (for strains M14459, NZ98/254, M13520) and ≥ 16 (for strain 96217) is $\geq 75\%$ for each of the M14459, 96217, NZ98/254, M13520 test strains. This outcome measure evaluated immune response to the rMenB+OMV NZ vaccine only, hence it was not applicable to the Placebo+PCV group. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

End point type	Primary
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End point timeframe:

At Day 331 (1 month after the fourth vaccination)

Notes:

[21] - 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: The analysis of this primary endpoint was descriptive i.e. No statistical hypothesis test was performed.

[22] - 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: This outcome measure evaluated immune response to the rMenB+OMV NZ vaccine only, hence it was not applicable to the Placebo+PCV group.

End point values	MenB+PCV Group			
Subject group type	Reporting group			
Number of subjects analysed	505			
Units: Percentage of participants				
number (confidence interval 95.8%)				
M14459 (fHbp)	89.0 (85.8 to 91.7)			
96217 (NadA)	99.6 (98.5 to 100)			
NZ98/254 (PorA P1.4)	83.2 (79.4 to 86.5)			
M13520 (NHBA)	76.6 (72.5 to 80.4)			

Statistical analyses

No statistical analyses for this end point

Primary: Adjusted Geometric Mean Concentrations (GMCs) of Immunoglobulin (IgG) Antibodies Against 13 PCV13 Antigens at 1 Month After Third Vaccination

End point title	Adjusted Geometric Mean Concentrations (GMCs) of Immunoglobulin (IgG) Antibodies Against 13 PCV13 Antigens at 1 Month After Third Vaccination
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End point description:

The immune response to PCV13 is evaluated by measuring IgG levels using electrochemiluminescence (ECL) assay. Adjusted GMCs are assessed for each of the 13 PCV13 antigens at 1 month after the third

vaccination. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

End point type	Primary
End point timeframe:	
At Day 151 (1 month after the third vaccination)	

End point values	MenB+PCV Group	Placebo+PCV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	244	278		
Units: Microgram per milliliter(µg/mL)				
geometric mean (confidence interval 98.3%)				
Serotype 1	1.6 (1.4 to 1.9)	1.5 (1.3 to 1.8)		
Serotype 3	0.5 (0.4 to 0.6)	0.5 (0.4 to 0.6)		
Serotype 4	1.1 (0.9 to 1.3)	1.1 (1.0 to 1.3)		
Serotype 5	1.0 (0.8 to 1.2)	1.0 (0.8 to 1.2)		
Serotype 6	2.4 (2.0 to 2.8)	2.5 (2.1 to 2.9)		
Serotype 6B	1.5 (1.1 to 1.9)	1.8 (1.4 to 2.3)		
Serotype 7F	2.8 (2.4 to 3.3)	2.9 (2.5 to 3.3)		
Serotype 9V	1.3 (1.1 to 1.6)	1.4 (1.2 to 1.6)		
Serotype 14	5.9 (4.7 to 7.4)	5.8 (4.8 to 7.2)		
Serotype 18C	1.5 (1.3 to 1.8)	1.5 (1.3 to 1.8)		
Serotype 19A	1.7 (1.4 to 2.0)	1.8 (1.6 to 2.2)		
Serotype 19F	2.5 (2.1 to 2.9)	2.5 (2.2 to 2.9)		
Serotype 23F	0.9 (0.7 to 1.1)	1.0 (0.8 to 1.2)		

Statistical analyses

Statistical analysis title	Between-group analysis
Statistical analysis description:	
To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone without rMenB+OMV NZ, at one month after the third vaccination.	
Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Group GMC Ratio
Point estimate	1.05
Confidence interval	
level	Other: 98.3 %
sides	2-sided
lower limit	0.9
upper limit	1.23

Statistical analysis title	Between-group analysis
Statistical analysis description:	
To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone without rMenB+OMV NZ, at one month after the third vaccination.	
Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Group GMC Ratio
Point estimate	0.9
Confidence interval	
level	Other: 98.3 %
sides	2-sided
lower limit	0.77
upper limit	1.06

Statistical analysis title	Between-group analysis
Statistical analysis description:	
To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone without rMenB+OMV NZ, at one month after the third vaccination.	
Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Group GMC Ratio
Point estimate	0.95
Confidence interval	
level	Other: 98.3 %
sides	2-sided
lower limit	0.81
upper limit	1.11

Statistical analysis title	Between-group analysis
Statistical analysis description:	
To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone without rMenB+OMV NZ, at one month after the third vaccination.	
Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Group GMC Ratio
Point estimate	1.01

Confidence interval	
level	Other: 98.3 %
sides	2-sided
lower limit	0.82
upper limit	1.24

Statistical analysis title	Between-group analysis
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Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone without rMenB+OMV NZ, at one month after the third vaccination.

Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Group GMC Ratio
Point estimate	0.8
Confidence interval	
level	Other: 98.3 %
sides	2-sided
lower limit	0.63
upper limit	1.02

Statistical analysis title	Between-group analysis
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Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone without rMenB+OMV NZ, at one month after the third vaccination.

Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Group GMC Ratio
Point estimate	0.98
Confidence interval	
level	Other: 98.3 %
sides	2-sided
lower limit	0.85
upper limit	1.12

Statistical analysis title	Between-group analysis
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Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone without rMenB+OMV NZ, at one month after the third vaccination.

Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Group GMC Ratio
Point estimate	1.03
Confidence interval	
level	Other: 98.3 %
sides	2-sided
lower limit	0.86
upper limit	1.22

Statistical analysis title	Between-group analysis
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Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone without rMenB+OMV NZ, at one month after the third vaccination.

Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Group GMC Ratio
Point estimate	0.98
Confidence interval	
level	Other: 98.3 %
sides	2-sided
lower limit	0.84
upper limit	1.15

Statistical analysis title	Between-group analysis
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Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone without rMenB+OMV NZ, at one month after the third vaccination.

Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Group GMC Ratio
Point estimate	0.94
Confidence interval	
level	Other: 98.3 %
sides	2-sided
lower limit	0.8
upper limit	1.12

Statistical analysis title	Between-group analysis
Statistical analysis description:	
To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone without rMenB+OMV NZ, at one month after the third vaccination.	
Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Group GMC Ratio
Point estimate	0.91
Confidence interval	
level	Other: 98.3 %
sides	2-sided
lower limit	0.77
upper limit	1.06

Statistical analysis title	Between-group analysis
Statistical analysis description:	
To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone without rMenB+OMV NZ, at one month after the third vaccination.	
Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Group GMC Ratio
Point estimate	1
Confidence interval	
level	Other: 98.3 %
sides	2-sided
lower limit	0.85
upper limit	1.18

Statistical analysis title	Between-group analysis
Statistical analysis description:	
To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone without rMenB+OMV NZ, at one month after the third vaccination.	
Comparison groups	MenB+PCV Group v Placebo+PCV Group

Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Group GMC Ratio
Point estimate	0.99
Confidence interval	
level	Other: 98.3 %
sides	2-sided
lower limit	0.86
upper limit	1.14

Statistical analysis title	Between-group analysis
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Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone without rMenB+OMV NZ, at one month after the third vaccination.

Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Group GMC Ratio
Point estimate	0.87
Confidence interval	
level	Other: 98.3 %
sides	2-sided
lower limit	0.73
upper limit	1.05

Secondary: Adjusted GMCs of IgG Antibodies Against 13 PCV13 Antigens at 1 Month after the fourth vaccination administered at Day 301

End point title	Adjusted GMCs of IgG Antibodies Against 13 PCV13 Antigens at 1 Month after the fourth vaccination administered at Day 301
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End point description:

The immune response to PCV13 is evaluated by measuring IgG levels using ECL assay. Adjusted GMCs are assessed for each of the 13 PCV13 antigens at 1 month after the fourth vaccination. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

End point type	Secondary
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End point timeframe:

At Day 331 (1 month after the fourth vaccination)

End point values		MenB+PCV Group	Placebo+PCV Group		
Subject group type		Reporting group	Reporting group		
Number of subjects analysed		225	240		
Units: µg/mL					
geometric mean (confidence interval 95%)					
	Serotype 1	1.8 (1.5 to 2.1)	1.8 (1.6 to 2.1)		
	Serotype 3	0.5 (0.4 to 0.6)	0.5 (0.5 to 0.6)		
	Serotype 4	1.5 (1.2 to 1.8)	1.7 (1.4 to 2.0)		
	Serotype 5	1.8 (1.5 to 2.1)	1.8 (1.6 to 2.1)		
	Serotype 6	5.2 (4.4 to 6.1)	6.0 (5.2 to 7.0)		
	Serotype 6B	4.7 (3.9 to 5.6)	5.4 (4.6 to 6.4)		
	Serotype 7F	3.7 (3.2 to 4.4)	4.6 (4.0 to 5.3)		
	Serotype 9V	2.3 (2.0 to 2.8)	2.6 (2.2 to 3.1)		
	Serotype 14	7.0 (5.8 to 8.4)	7.1 (6.0 to 8.4)		
	Serotype 18C	2.0 (1.7 to 2.4)	2.2 (1.9 to 2.6)		
	Serotype 19A	4.5 (3.8 to 5.3)	5.5 (4.7 to 6.4)		
	Serotype 19F	4.8 (4.1 to 5.7)	5.0 (4.3 to 5.9)		
	Serotype 23F	1.9 (1.5 to 2.3)	1.9 (1.6 to 2.3)		

Statistical analyses

Statistical analysis title	Between-group analysis
Statistical analysis description:	
To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone, at one month after the fourth vaccination.	
Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	465
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Group GMC Ratio
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.07

Statistical analysis title		Between-group analysis
Statistical analysis description:		
To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone, at one month after the fourth vaccination.		
Comparison groups	MenB+PCV Group v Placebo+PCV Group	

Number of subjects included in analysis	465
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Group GMC Ratio
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	1.03

Statistical analysis title	Between-group analysis
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Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone, at one month after the fourth vaccination.

Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	465
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Group GMC Ratio
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.11

Statistical analysis title	Between-group analysis
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Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone, at one month after the fourth vaccination.

Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	465
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Group GMC Ratio
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.16

Statistical analysis title	Between-group analysis
Statistical analysis description:	
To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone, at one month after the fourth vaccination.	
Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	465
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Group GMC Ratio
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.06

Statistical analysis title	Between-group analysis
Statistical analysis description:	
To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone, at one month after the fourth vaccination.	
Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	465
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Group GMC Ratio
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.17

Statistical analysis title	Between-group analysis
Statistical analysis description:	
To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone, at one month after the fourth vaccination.	
Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	465
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Group GMC Ratio
Point estimate	0.89

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1.04

Statistical analysis title	Between-group analysis
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Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone, at one month after the fourth vaccination.

Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	465
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Group GMC Ratio
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	0.95

Statistical analysis title	Between-group analysis
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Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone, at one month after the fourth vaccination.

Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	465
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Group GMC Ratio
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.12

Statistical analysis title	Between-group analysis
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Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone, at one month after the fourth vaccination.

Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	465
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Group GMC Ratio
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.02

Statistical analysis title	Between-group analysis
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Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone, at one month after the fourth vaccination.

Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	465
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Group GMC Ratio
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	0.99

Statistical analysis title	Between-group analysis
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Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone, at one month after the fourth vaccination.

Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	465
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Group GMC Ratio
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.12

Statistical analysis title	Between-group analysis
Statistical analysis description: To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone, at one month after the fourth vaccination.	
Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	465
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Group GMC Ratio
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	0.93

Secondary: Percentage of participants with serum pneumococcal anti-capsular polysaccharide IgG $\geq 0.35 \mu\text{g/mL}$

End point title	Percentage of participants with serum pneumococcal anti-capsular polysaccharide IgG $\geq 0.35 \mu\text{g/mL}$
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End point description:

The immune response to PCV13 is evaluated by measuring the percentage of participants with serum IgG concentrations $\geq 0.35 \mu\text{g/mL}$ for each of the 13 PCV13 antigens at 1 month after the third and fourth vaccinations. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

End point type	Secondary
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End point timeframe:

At Day 151 (1 month after the third vaccination) and Day 331 (1 month after the fourth vaccination)

End point values	MenB+PCV Group	Placebo+PCV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	244	278		
Units: Percentage of participants				
number (confidence interval 95%)				
Serotype 1, At Day 151	99.2 (97.1 to 99.9)	97.1 (94.4 to 98.7)		
Serotype 1, At Day 331	98.7 (96.2 to 99.7)	97.1 (94.1 to 98.8)		
Serotype 3, At Day 151	59.8 (53.4 to 66.0)	61.5 (55.5 to 67.3)		
Serotype 3, At Day 331	63.6 (56.9 to 69.8)	69.5 (63.2 to 75.2)		
Serotype 4, At Day 151	94.3 (90.6 to 96.8)	96.0 (93.0 to 98.0)		

Serotype 4, At Day 331	97.8 (94.9 to 99.3)	96.7 (93.5 to 98.6)		
Serotype 5, At Day 151	91.0 (86.7 to 94.3)	87.4 (82.9 to 91.1)		
Serotype 5, At Day 331	96.0 (92.5 to 98.2)	98.8 (96.4 to 99.7)		
Serotype 6, At Day 151	99.2 (97.1 to 99.9)	99.6 (98.0 to 100)		
Serotype 6, At Day 331	100 (98.4 to 100)	99.6 (97.7 to 100)		
Serotype 6B, At Day 151	89.8 (85.2 to 93.3)	92.4 (88.7 to 95.3)		
Serotype 6B, At Day 331	100 (98.4 to 100)	99.6 (97.7 to 100)		
Serotype 7F, At Day 151	99.6 (97.7 to 100)	100 (98.7 to 100)		
Serotype 7F, At Day 331	99.6 (97.5 to 100)	100 (98.5 to 100)		
Serotype 9V, At Day 151	95.1 (91.6 to 97.4)	93.2 (89.5 to 95.8)		
Serotype 9V, At Day 331	98.7 (96.1 to 99.7)	98.8 (96.4 to 99.7)		
Serotype 14, At Day 151	98.0 (95.3 to 99.3)	98.6 (96.4 to 99.6)		
Serotype 14, At Day 331	100 (98.4 to 100)	100 (98.5 to 100)		
Serotype 18C, At Day 151	97.5 (94.7 to 99.1)	96.8 (93.9 to 98.5)		
Serotype 18C, At Day 331	99.1 (96.8 to 99.9)	99.2 (97.0 to 99.9)		
Serotype 19A, At Day 151	96.7 (93.6 to 98.6)	98.6 (96.4 to 99.6)		
Serotype 19A, At Day 331	100 (98.4 to 100)	99.6 (97.7 to 100)		
Serotype 19F, At Day 151	99.6 (97.7 to 100)	100 (98.7 to 100)		
Serotype 19F, At Day 331	100 (98.4 to 100)	100 (98.5 to 100)		
Serotype 23F, At Day 151	87.3 (82.5 to 91.2)	87.0 (82.5 to 90.7)		
Serotype 23F, At Day 331	97.3 (94.3 to 99.0)	97.1 (94.1 to 98.8)		

Statistical analyses

Statistical analysis title	Between-group analysis
Statistical analysis description:	
To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone, at one month after the third vaccination.	
Comparison groups	MenB+PCV Group v Placebo+PCV Group

Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage
Point estimate	2.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.38
upper limit	4.87

Statistical analysis title	Between-group analysis
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Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone, at one month after the fourth vaccination.

Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage
Point estimate	1.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.28
upper limit	4.74

Statistical analysis title	Between-group analysis
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Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the third vaccination.

Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage
Point estimate	-0.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.29
upper limit	0.96

Statistical analysis title	Between-group analysis
Statistical analysis description:	
To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the fourth vaccination.	
Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage
Point estimate	0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.27
upper limit	2.33

Statistical analysis title	Between-group analysis
Statistical analysis description:	
To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the third vaccination.	
Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage
Point estimate	-2.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.86
upper limit	2.21

Statistical analysis title	Between-group analysis
Statistical analysis description:	
To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the fourth vaccination.	
Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage
Point estimate	0.42

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.27
upper limit	2.33

Statistical analysis title	Between-group analysis
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Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the third vaccination.

Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage
Point estimate	-0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.62
upper limit	1.27

Statistical analysis title	Between-group analysis
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Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the fourth vaccination.

Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage
Point estimate	-2.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.33
upper limit	0.16

Statistical analysis title	Between-group analysis
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Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the third vaccination.

Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage
Point estimate	3.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.86
upper limit	8.96

Statistical analysis title	Between-group analysis
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Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the fourth vaccination.

Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage
Point estimate	1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.17
upper limit	4.51

Statistical analysis title	Between-group analysis
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Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the third vaccination.

Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage
Point estimate	-1.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.87
upper limit	1.97

Statistical analysis title	Between-group analysis
Statistical analysis description:	
To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone, at one month after the fourth vaccination.	
Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage
Point estimate	-5.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14.45
upper limit	2.69

Statistical analysis title	Between-group analysis
Statistical analysis description:	
To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV, compared to PCV13 and other RIV alone, at one month after the third vaccination.	
Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage
Point estimate	-1.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.07
upper limit	6.7

Statistical analysis title	Between-group analysis
Statistical analysis description:	
To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the fourth vaccination.	
Comparison groups	MenB+PCV Group v Placebo+PCV Group

Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage
Point estimate	-0.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.48
upper limit	1.14

Statistical analysis title	Between-group analysis
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Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the third vaccination.

Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage
Point estimate	0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.62
upper limit	6.07

Statistical analysis title	Between-group analysis
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Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the fourth vaccination.

Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.68
upper limit	1.58

Statistical analysis title	Between-group analysis
Statistical analysis description:	
To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the third vaccination.	
Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage
Point estimate	-0.41
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.29
upper limit	0.96

Statistical analysis title	Between-group analysis
Statistical analysis description:	
To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the fourth vaccination.	
Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage
Point estimate	0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.27
upper limit	2.33

Statistical analysis title	Between-group analysis
Statistical analysis description:	
To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the third vaccination.	
Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage
Point estimate	-1.84

Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.06
upper limit	0.83

Statistical analysis title	Between-group analysis
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Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the fourth vaccination.

Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage
Point estimate	0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.13
upper limit	3.58

Statistical analysis title	Between-group analysis
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Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the third vaccination.

Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage
Point estimate	0.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4
upper limit	3.91

Statistical analysis title	Between-group analysis
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Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the fourth vaccination.

Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.68
upper limit	1.58

Statistical analysis title	Between-group analysis
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Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the third vaccination.

Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage
Point estimate	-0.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.43
upper limit	1.87

Statistical analysis title	Between-group analysis
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Statistical analysis description:

To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the fourth vaccination.

Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage
Point estimate	-0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.76
upper limit	2.44

Statistical analysis title	Between-group analysis
Statistical analysis description:	
To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the third vaccination.	
Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage
Point estimate	1.92
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	6.12

Statistical analysis title	Between-group analysis
Statistical analysis description:	
To demonstrate the immunological non-inferiority of PCV13 when administered concomitantly with rMenB+OMV NZ and other RIV compared to PCV13 and other RIV alone, at one month after the fourth vaccination.	
Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	522
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage
Point estimate	-0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.44
upper limit	2.2

Secondary: Adjusted GMCs against 3 pertussis antigens (pertussis toxin [PT], pertactin [PRN], filamentous hemagglutinin [FHA])

End point title	Adjusted GMCs against 3 pertussis antigens (pertussis toxin [PT], pertactin [PRN], filamentous hemagglutinin [FHA])
End point description:	
The immune response to DTaP-HBV-IPV (Pediarix) vaccine is evaluated. IgG concentrations for pertussis antigens (PT, FHA, PRN) are measured at 1 month after the third vaccination and are expressed as international units per millilitre (IU/mL). Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.	
End point type	Secondary

End point timeframe:

At Day 151 (1 month after the third vaccination)

End point values	MenB+PCV Group	Placebo+PCV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	470	266		
Units: IU/mL				
geometric mean (confidence interval 95%)				
PT	50.3 (45.1 to 56.0)	59.6 (53.2 to 66.8)		
FHA	106.7 (96.4 to 118.0)	133.1 (119.5 to 148.2)		
Pertactin	41.7 (36.1 to 48.1)	65.7 (56.4 to 76.4)		

Statistical analyses

Statistical analysis title	Between-group analysis
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Statistical analysis description:

To demonstrate the immunological non-inferiority of DTaP-HBV-IPV vaccine when administered concomitantly with rMenB+OMV NZ and PCV13 compared to DTaP-HBV-IPV vaccine concomitantly administered with PCV13 without rMenB+OMV NZ, in terms of PT, FHA and PRN, at one month after the third vaccination.

Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	736
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Group GMC Ratio
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	0.94

Statistical analysis title	Between-group analysis
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Statistical analysis description:

To demonstrate the immunological non-inferiority of DTaP-HBV-IPV vaccine when administered concomitantly with rMenB+OMV NZ and PCV13 compared to DTaP-HBV-IPV vaccine concomitantly administered with PCV13 without rMenB+OMV NZ, in terms of PT, FHA and PRN, at one month after the third vaccination.

Comparison groups	MenB+PCV Group v Placebo+PCV Group
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Number of subjects included in analysis	736
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Group GMC Ratio
Point estimate	0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	0.73

Statistical analysis title	Between-group analysis
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Statistical analysis description:

To demonstrate the immunological non-inferiority of DTaP-HBV-IPV vaccine when administered concomitantly with rMenB+OMV NZ and PCV13 compared to DTaP-HBV-IPV vaccine concomitantly administered with PCV13 without rMenB+OMV NZ, in terms of PT, FHA and PRN, at one month after the third vaccination.

Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	736
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Group GMC Ratio
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	0.88

Secondary: Percentage of participants with antibodies concentrations against hepatitis B surface antigen (AntiHBsAg) $\geq$ 10 mIU/mL

End point title	Percentage of participants with antibodies concentrations against hepatitis B surface antigen (AntiHBsAg) $\geq$ 10 mIU/mL
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End point description:

The immune response to DTaP-HBV-IPV vaccine administered with rMenB+OMV NZ and PCV13 is evaluated. IgG concentrations for Hepatitis B (HepB) antigens are measured at 1 month after the third vaccination. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

End point type	Secondary
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End point timeframe:

At Day 151 (1 month after the third vaccination)

End point values	MenB+PCV Group	Placebo+PCV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	138		
Units: Percentage of participants				
number (confidence interval 95%)	100 (96.5 to 100)	99.3 (96.0 to 100)		

Statistical analyses

Statistical analysis title	Between-group analysis
Statistical analysis description:	
To demonstrate the immunological non-inferiority of DTaP-HBV-IPV vaccine when administered concomitantly with rMenB+OMV NZ and PCV13 compared to DTaP-HBV-IPV vaccine concomitantly administered with PCV13 without rMenB+OMV NZ, in terms of Hep B, at one month after the third vaccination.	
Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	243
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.83
upper limit	4

Secondary: Percentage of participants with anti-diphtheria and anti-tetanus antibody concentrations ≥ 0.1 IU/mL

End point title	Percentage of participants with anti-diphtheria and anti-tetanus antibody concentrations ≥ 0.1 IU/mL
End point description:	
The immune response to DTaP-HBV-IPV vaccine administered with rMenB+OMV NZ and PCV13 is evaluated. IgG concentrations for diphtheria (D) and tetanus (T) were measured at 1 month after the third vaccination. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.	
End point type	Secondary
End point timeframe:	
At Day 151 (1 month after the third vaccination)	

End point values	MenB+PCV Group	Placebo+PCV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	224	143		
Units: Percentage of participants				
number (confidence interval 95%)				
Tetanus Toxoid	100 (98.4 to 100)	100 (97.5 to 100)		
Diphtheria Toxoid	99.5 (97.5 to 100)	100 (97.3 to 100)		

Statistical analyses

Statistical analysis title	Between-group analysis
Statistical analysis description:	
To demonstrate the immunological non-inferiority of DTaP-HBV-IPV vaccine when administered concomitantly with rMenB+OMV NZ and PCV13 compared to DTaP-HBV-IPV vaccine concomitantly administered with PCV13 without rMenB+OMV NZ, in terms of T, at one month after the third vaccination.	
Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage
Point estimate	-0.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.53
upper limit	2.3

Statistical analysis title	Between-group analysis
Statistical analysis description:	
To demonstrate the immunological non-inferiority of DTaP-HBV-IPV vaccine when administered concomitantly with rMenB+OMV NZ and PCV13 compared to DTaP-HBV-IPV vaccine concomitantly administered with PCV13 without rMenB+OMV NZ, in terms of D, at one month after the third vaccination.	
Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	367
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.69
upper limit	2.62

Secondary: Percentage of participants with anti-polyribosyl-ribitol phosphate (PRP) concentration $\geq 0.15 \mu\text{g/mL}$ and $\geq 1 \mu\text{g/mL}$

End point title	Percentage of participants with anti-polyribosyl-ribitol phosphate (PRP) concentration $\geq 0.15 \mu\text{g/mL}$ and $\geq 1 \mu\text{g/mL}$
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End point description:

The immune response to Hib vaccine administered with rMenB+OMV NZ and PCV13 is evaluated. IgG concentrations for Haemophilus influenzae type b (Hib) are measured at 1 month after the third vaccination. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

End point type	Secondary
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End point timeframe:

At Day 151 (1 month after the third vaccination)

End point values	MenB+PCV Group	Placebo+PCV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	347	264		
Units: Percentage of participants				
number (confidence interval 95%)				
$\geq 0.15 \mu\text{g/mL}$	98.3 (96.3 to 99.4)	97.7 (95.1 to 99.2)		
$\geq 1 \mu\text{g/mL}$	87.0 (83.0 to 90.4)	84.1 (79.1 to 88.3)		

Statistical analyses

Statistical analysis title	Between-group analysis
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Statistical analysis description:

To demonstrate the immunological non-inferiority of Hib vaccine when administered concomitantly with rMenB+OMV NZ and PCV13 compared to Hib vaccine concomitantly administered with PCV13 without rMenB+OMV NZ, in terms of Hib, at one month after the third vaccination.

Comparison groups	MenB+PCV Group v Placebo+PCV Group
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Number of subjects included in analysis	611
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Analysis specification	Pre-specified
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Analysis type	
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Parameter estimate	Difference in percentage
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Point estimate	2.94
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Confidence interval

level	95 %
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sides	2-sided
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lower limit	-2.63
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upper limit	8.78
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Statistical analysis title	Between-group analysis
Statistical analysis description: To demonstrate the immunological non-inferiority of Hib vaccine when administered concomitantly with rMenB+OMV NZ and PCV13 compared to Hib vaccine concomitantly administered with PCV13 without rMenB+OMV NZ, in terms of Hib, at one month after the third vaccination.	
Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	611
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Difference in percentage
Point estimate	0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.79
upper limit	3.32

Secondary: Adjusted GMCs for anti-measles antibodies

End point title	Adjusted GMCs for anti-measles antibodies
End point description: The immune response to MMR vaccine administered with rMenB+OMV NZ and PCV13 is evaluated. IgG concentrations for measles antigens are measured using adjusted GMCs at 1 month after fourth vaccination and are expressed as milli-International Units per milliliter (mIU/mL). Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.	
End point type	Secondary
End point timeframe: At Day 331 (1 month after the fourth vaccination)	

End point values	MenB+PCV Group	Placebo+PCV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	435	235		
Units: mIU/mL				
geometric mean (confidence interval 95%)	877.3 (743.7 to 1035.0)	873.5 (732.2 to 1042.0)		

Statistical analyses

Statistical analysis title	Between-group analysis
Statistical analysis description: To demonstrate the immunological non-inferiority of MMR vaccine when administered concomitantly with rMenB+OMV NZ and PCV13 compared to MMR vaccine concomitantly administered with PCV13, without rMenB+OMV NZ, at one month after fourth vaccination.	
Comparison groups	MenB+PCV Group v Placebo+PCV Group

Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Group GMC Ratio
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.86
upper limit	1.17

Secondary: Adjusted GMCs for anti-mumps antibodies

End point title	Adjusted GMCs for anti-mumps antibodies
End point description:	The immune response to MMR vaccine administered with rMenB+OMV NZ and PCV13 is evaluated. IgG concentrations for mumps antigens are measured using adjusted GMCs at 1 month after fourth vaccination. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.
End point type	Secondary
End point timeframe:	At Day 331 (1 month after the fourth vaccination)

End point values	MenB+PCV Group	Placebo+PCV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	435	235		
Units: Arbitrary Units per milliliter (AU/mL)				
geometric mean (confidence interval 95%)	744.5 (628.5 to 882.0)	856.8 (715.0 to 1026.7)		

Statistical analyses

Statistical analysis title	Between-group analysis
Statistical analysis description:	To demonstrate the immunological non-inferiority of MMR vaccine when administered concomitantly with rMenB+OMV NZ and PCV13 compared to MMR vaccine concomitantly administered with PCV13, without rMenB+OMV NZ, at one month after fourth vaccination.
Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Group GMC Ratio
Point estimate	0.87

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.74
upper limit	1.02

Secondary: Adjusted GMCs for anti-rubella antibodies

End point title	Adjusted GMCs for anti-rubella antibodies
End point description:	
The immune response to MMR vaccine administered with rMenB+OMV NZ and PCV13 is evaluated. IgG concentrations for rubella antigens are measured using adjusted GMCs at 1 month after fourth vaccination. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.	
End point type	Secondary
End point timeframe:	
At Day 331 (1 month after the fourth vaccination)	

End point values	MenB+PCV Group	Placebo+PCV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	432	235		
Units: IU/mL				
geometric mean (confidence interval 95%)	57.7 (50.0 to 66.6)	54.0 (46.3 to 63.0)		

Statistical analyses

Statistical analysis title	Between-group analysis
Statistical analysis description:	
To demonstrate the immunological non-inferiority of MMR vaccine when administered concomitantly with rMenB+OMV NZ, VV and PCV13 compared to MMR vaccine concomitantly administered with PCV13, without rMenB+OMV NZ, at one month after fourth vaccination.	
Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	667
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Group GMC Ratio
Point estimate	1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	1.22

Secondary: Adjusted GMCs for anti-Varicella (VV) antibodies

End point title	Adjusted GMCs for anti-Varicella (VV) antibodies
End point description: The immune response to varicella (VV) vaccine administered with rMenB+OMV NZ and PCV13 is evaluated. IgG concentrations for varicella antigens are measured using GMCs at 1 month after fourth vaccination. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.	
End point type	Secondary
End point timeframe: At Day 331 (1 month after the fourth vaccination)	

End point values	MenB+PCV Group	Placebo+PCV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	437	231		
Units: mIU/mL				
geometric mean (confidence interval 95%)	1283.8 (1137.4 to 1449.2)	1208.9 (1060.5 to 1378.2)		

Statistical analyses

Statistical analysis title	Between-group analysis
Statistical analysis description: To demonstrate the immunological non-inferiority of VV vaccine when administered concomitantly with rMenB+OMV NZ, MMR and PCV13 compared to VV vaccine concomitantly administered with PCV13, without rMenB+OMV NZ, at one month after fourth vaccination.	
Comparison groups	MenB+PCV Group v Placebo+PCV Group
Number of subjects included in analysis	668
Analysis specification	Pre-specified
Analysis type	
Parameter estimate	Group GMC Ratio
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	1.19

Secondary: Percentage of participants with hSBA antibody titers ≥ 5 , ≥ 8 and ≥ 16 for each of the Serogroup B Test Strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4), and M13520 (NHBA)

End point title	Percentage of participants with hSBA antibody titers ≥ 5 , ≥ 8 and ≥ 16 for each of the Serogroup B Test Strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4), and M13520 (NHBA) ^[23]
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End point description:

This immune response to the rMenB+OMV NZ vaccine only is evaluated, hence it was not applicable to the Placebo+PCV group. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

End point type	Secondary
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End point timeframe:

At Day 151 (1 month after the third vaccination)

Notes:

[23] - 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: This outcome measure evaluated immune response to the rMenB+OMV NZ vaccine only, hence it was not applicable to the Placebo+PCV group.

End point values	MenB+PCV Group			
Subject group type	Reporting group			
Number of subjects analysed	553			
Units: Percentage of participants				
number (confidence interval 95%)				
M14459 (fHbp), ≥ 5	92.2 (89.6 to 94.3)			
M14459 (fHbp), ≥ 8	82.9 (79.4 to 86.0)			
M14459 (fHbp), ≥ 16	50.5 (46.2 to 54.8)			
96217 (NadA), ≥ 5	99.6 (98.6 to 100)			
96217 (NadA), ≥ 8	99.6 (98.6 to 100)			
96217 (NadA), ≥ 16	99.4 (98.3 to 99.9)			
NZ98/254 (PorA P1.4), ≥ 5	77.7 (74.0 to 81.1)			
NZ98/254 (PorA P1.4), ≥ 8	61.8 (57.6 to 65.9)			
NZ98/254 (PorA P1.4), ≥ 16	31.1 (27.2 to 35.1)			
M13520 (NHBA), ≥ 5	60.4 (56.2 to 64.5)			
M13520 (NHBA), ≥ 8	32.4 (28.5 to 36.4)			
M13520 (NHBA), ≥ 16	9.4 (7.1 to 12.1)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with hSBA antibody titers ≥ 5 and ≥ 8 for each of the Serogroup B Test Strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4), and M13520 (NHBA)

End point title	Percentage of participants with hSBA antibody titers ≥ 5 and ≥ 8 for each of the Serogroup B Test Strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4), and M13520 (NHBA) ^[24]
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End point description:

This immune response to the rMenB+OMV NZ vaccine only is evaluated, hence it was not applicable to the Placebo+PCV group. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

End point type	Secondary
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End point timeframe:

At Day 301 (6 months after third vaccination)

Notes:

[24] - 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: This outcome measure evaluated immune response to the rMenB+OMV NZ vaccine only, hence it was not applicable to the Placebo+PCV group.

End point values	MenB+PCV Group			
Subject group type	Reporting group			
Number of subjects analysed	540			
Units: Percentage of participants				
number (confidence interval 95%)				
M14459 (fHbp), ≥ 5	14.5 (11.6 to 17.9)			
M14459 (fHbp), ≥ 8	4.8 (3.2 to 7.1)			
96217 (NadA) ≥ 5	97.8 (96.1 to 98.9)			
96217 (NadA), ≥ 8	96.4 (94.4 to 97.9)			
NZ98/254 (PorA P1.4), ≥ 5	20.2 (16.8 to 23.8)			
NZ98/254 (PorA P1.4), ≥ 8	12.2 (9.6 to 15.3)			
M13520 (NHBA), ≥ 5	10.2 (7.8 to 13.1)			
M13520 (NHBA) ≥ 8	5.9 (4.1 to 8.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with hSBA antibody titers ≥ 5 for each of the Serogroup B Test Strain M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4), and M13520 (NHBA)

End point title	Percentage of participants with hSBA antibody titers ≥ 5 for each of the Serogroup B Test Strain M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4), and M13520 (NHBA) ^[25]
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End point description:

This immune response to the rMenB+OMV NZ vaccine only is evaluated, hence it was not applicable to the Placebo+PCV group. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

End point type	Secondary
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End point timeframe:

At Day 331 (1 month after the fourth vaccination)

Notes:

[25] - 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: This outcome measure evaluated immune response to the rMenB+OMV NZ vaccine only, hence it was not applicable to the Placebo+PCV group.

End point values	MenB+PCV Group			
Subject group type	Reporting group			
Number of subjects analysed	505			
Units: Percentage of participants				
number (confidence interval 95%)				
M14459 (fHbp), ≥ 5	94.5 (92.1 to 96.4)			
96217 (NadA), ≥ 5	99.6 (98.5 to 99.9)			
NZ98/254 (PorA P1.4), ≥ 5	89.6 (86.6 to 92.1)			
M13520 (NHBA), ≥ 5	91.5 (88.7 to 93.8)			

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA Geometric Mean Titers (GMTs) against each of the Serogroup B Test Strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4), and M13520 (NHBA)

End point title	hSBA Geometric Mean Titers (GMTs) against each of the Serogroup B Test Strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4), and M13520 (NHBA) ^[26]
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End point description:

This immune response to the rMenB+OMV NZ vaccine only is evaluated, hence it was not applicable to the Placebo+PCV group. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

End point type	Secondary
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End point timeframe:

At Day 151 (1 month after the third vaccination), Day 301 (6 months after the third vaccination), and Day 331 (1 month after the fourth vaccination)

Notes:

[26] - 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: This outcome measure evaluated immune response to the rMenB+OMV NZ vaccine only, hence it was not applicable to the Placebo+PCV group.

End point values	MenB+PCV Group			
Subject group type	Reporting group			
Number of subjects analysed	553			
Units: Titer				
geometric mean (confidence interval 95%)				
M14459 (fHbp), Day 151	15.1 (13.7 to 16.7)			

M14459 (fHbp), Day 301	3.0 (2.8 to 3.2)			
M14459 (fHbp), Day 331	24.3 (21.3 to 27.8)			
96217 (NadA), Day 151	488.2 (437.3 to 545.0)			
96217 (NadA), Day 301	89.1 (77.3 to 102.7)			
96217 (NadA), Day 331	1349.0 (1195.3 to 1522.5)			
NZ98/254 (PorA P1.4), Day 151	10.1 (8.9 to 11.4)			
NZ98/254 (PorA P1.4), Day 301	3.8 (3.5 to 4.0)			
NZ98/254 (PorA P1.4), Day 331	20.3 (17.3 to 23.7)			
M13520 (NHBA), Day 151	5.5 (5.0 to 6.0)			
M13520 (NHBA), Day 301	3.5 (3.3 to 3.7)			
M13520 (NHBA), Day 331	12.7 (11.2 to 14.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA Geometric Mean Ratios (GMRs) over pre fourth vaccination against each of the Serogroup B Test Strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4), and M13520 (NHBA)

End point title	hSBA Geometric Mean Ratios (GMRs) over pre fourth vaccination against each of the Serogroup B Test Strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4), and M13520 (NHBA) ^[27]
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End point description:

This immune response to the rMenB+OMV NZ vaccine only is evaluated, hence it was not applicable to the Placebo+PCV group. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

End point type	Secondary
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End point timeframe:

At Day 331 (1 month after the fourth vaccination) compared to Day 301 (pre-fourth vaccination)

Notes:

[27] - 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: This outcome measure evaluated immune response to the rMenB+OMV NZ vaccine only, hence it was not applicable to the Placebo+PCV group.

End point values	MenB+PCV Group			
Subject group type	Reporting group			
Number of subjects analysed	465			
Units: Ratio				
geometric mean (confidence interval 95%)				
M14459 (fHbp)	8.7 (7.6 to 10.0)			
96217 (NadA)	17.4 (15.1 to 20.1)			

NZ98/254 (PorA P1.4)	5.5 (4.7 to 6.5)			
M13520 (NHBA)	3.9 (3.4 to 4.4)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with hSBA antibody titers $\geq$ LLOQ for each of the Serogroup B test strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4), and M13520 (NHBA)

End point title	Percentage of participants with hSBA antibody titers $\geq$ LLOQ for each of the Serogroup B test strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4), and M13520 (NHBA) ^[28]
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End point description:

This immune response to the rMenB+OMV NZ vaccine only is evaluated, hence it was not applicable to the Placebo+PCV group. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

End point type	Secondary
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End point timeframe:

At Day 301 (6 months after the third vaccination) and Day 331 (1 month after the fourth vaccination)

Notes:

[28] - 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: This outcome measure evaluated immune response to the rMenB+OMV NZ vaccine only, hence it was not applicable to the Placebo+PCV group.

End point values	MenB+PCV Group			
Subject group type	Reporting group			
Number of subjects analysed	540			
Units: Percentage of participants				
number (confidence interval 95%)				
M14459 (fHbp), Day 301	14.5 (11.6 to 17.9)			
M14459 (fHbp), Day 331	94.5 (92.1 to 96.4)			
96217 (NadA), Day 301	94.1 (91.6 to 96.0)			
96217 (NadA), Day 331	99.6 (98.5 to 99.9)			
M13520 (NHBA), Day 301	8.5 (6.3 to 11.2)			
M13520 (NHBA), Day 331	86.1 (82.8 to 89.0)			
NZ98/254 (PorA P1.4), Day 301	17.5 (14.4 to 21.0)			
NZ98/254 (PorA P1.4), Day 331	87.6 (84.4 to 90.3)			

Statistical analyses

Secondary: Percentage of participants with 4-fold rise in hSBA titers for each of the Serogroup B Test Strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4), and M13520 (NHBA)

End point title	Percentage of participants with 4-fold rise in hSBA titers for each of the Serogroup B Test Strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4), and M13520 (NHBA) ^[29]
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End point description:

A 4-fold rise in hSBA titers is defined as - if pre-vaccination titer <Limit of Detection (LOD), then a post-vaccination titer ≥ 4 times the LOD or $\geq$ LLOQ, whichever is greater; - if pre-vaccination titer is $\geq$ LOD but <LLOQ, then a post-vaccination titer ≥ 4 times the LLOQ; - if pre-vaccination titer is $\geq$ LLOQ, then a post-vaccination titer ≥ 4 times the pre-vaccination titer, where pre-vaccination titer=pre-4th dose titers (Day 301). This outcome measure evaluated immune response to the rMenB+OMV NZ vaccine only, hence it was not applicable to the Placebo+PCV group. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

End point type	Secondary
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End point timeframe:

At Day 331 (1 month after the fourth vaccination) relative to Day 301 (pre-fourth vaccination)

Notes:

[29] - 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: This outcome measure evaluated immune response to the rMenB+OMV NZ vaccine only, hence it was not applicable to the Placebo+PCV group.

End point values	MenB+PCV Group			
Subject group type	Reporting group			
Number of subjects analysed	465			
Units: Percentage of participants				
number (confidence interval 95%)				
M14459 (fHbp), Day 331	72.0 (67.5 to 76.1)			
96217 (NadA), Day 331	94.8 (92.2 to 96.7)			
M13520 (NHBA), Day 331	36.1 (31.8 to 40.7)			
NZ98/254 (PorA P1.4), Day 331	54.2 (49.5 to 58.9)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with anti-HBs antibody concentrations ≥ 100 mIU/mL

End point title	Percentage of participants with anti-HBs antibody concentrations ≥ 100 mIU/mL
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End point description:

Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

End point type	Secondary
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End point timeframe:

At Day 151 (1 month after the third vaccination)

End point values	MenB+PCV Group	Placebo+PCV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	138		
Units: Percentage of participants				
number (confidence interval 95%)	98.1 (93.3 to 99.8)	96.4 (91.7 to 98.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: GMCs for Anti-HBsAg antibodies

End point title	GMCs for Anti-HBsAg antibodies
End point description: Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.	
End point type	Secondary
End point timeframe: At Day 151 (1 month after the third vaccination)	

End point values	MenB+PCV Group	Placebo+PCV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	105	138		
Units: mIU/mL				
geometric mean (confidence interval 95%)	2201.0 (1554.7 to 3116.0)	2404.8 (1803.1 to 3207.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with anti-diphtheria and anti-tetanus antibody concentrations ≥ 1 IU/mL

End point title	Percentage of participants with anti-diphtheria and anti-tetanus antibody concentrations ≥ 1 IU/mL
End point description: Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.	

End point type	Secondary
End point timeframe:	
At Day 151 (1 month after the third vaccination)	

End point values	MenB+PCV Group	Placebo+PCV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	224	143		
Units: Percentage of participants				
number (confidence interval 95%)				
Tetanus Toxoid	67.0 (60.4 to 73.1)	69.2 (61.0 to 76.7)		
Diphtheria Toxoid	40.0 (33.5 to 46.8)	55.1 (46.4 to 63.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: GMCs for anti-diphtheria and anti-tetanus antibodies

End point title	GMCs for anti-diphtheria and anti-tetanus antibodies
End point description:	
Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.	
End point type	Secondary
End point timeframe:	
At Day 151 (1 month after the third vaccination)	

End point values	MenB+PCV Group	Placebo+PCV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	224	143		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Tetanus Toxoid	1.5 (1.3 to 1.8)	1.6 (1.3 to 1.9)		
Diphtheria Toxoid	0.9 (0.8 to 1.1)	1.2 (1.0 to 1.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with anti-polio type 1, 2 and 3 neutralization

antibody titers ≥ 8

End point title	Percentage of participants with anti-polio type 1, 2 and 3 neutralization antibody titers ≥ 8
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End point description:

Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

End point type	Secondary
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End point timeframe:

At Day 151 (1 month after the third vaccination)

End point values	MenB+PCV Group	Placebo+PCV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	106	120		
Units: Percentage of participants				
number (confidence interval 95%)				
Polio 1	100 (96.4 to 100)	100 (97.0 to 100)		
Polio 2	99.1 (94.9 to 100)	100 (96.9 to 100)		
Polio 3	100 (96.3 to 100)	99.1 (95.1 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with seroresponse for anti-Varicella (VV), anti-measles virus, anti-mumps virus and anti-rubella virus antibodies

End point title	Percentage of participants with seroresponse for anti-Varicella (VV), anti-measles virus, anti-mumps virus and anti-rubella virus antibodies
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End point description:

Seroresponse is defined as post-vaccination anti-VZV virus, anti-measles virus, anti-mumps virus and anti-rubella virus antibody concentration $\geq$ a protective threshold among participants who were seronegative (antibody concentration $<$ assay cut-off) before vaccination. Analysis was performed on the PPS for immunogenicity. Only participants with data available at the specified timepoints were included in this analysis.

End point type	Secondary
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End point timeframe:

At Day 331 (1 month after the fourth vaccination)

End point values	MenB+PCV Group	Placebo+PCV Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	364	201		
Units: Percentage of participants				
number (confidence interval 95%)				
Mumps	81.6 (77.2 to 85.5)	85.9 (80.2 to 90.4)		
Measles	94.8 (91.9 to 96.9)	97.9 (94.7 to 99.4)		
Rubella	86.4 (82.3 to 89.8)	83.9 (78.1 to 88.7)		
VZV gE	97.3 (95.0 to 98.7)	97.5 (94.3 to 99.2)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited AEs: Day 1 to Day 7 post each vaccination, Solicited systemic AEs of salivary gland swelling, fever and rash: Day 1 to Day 30 post fourth vaccination; Unsolicited AEs: Day 1 to Day 30 post each vaccination.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	27.1

Reporting groups

Reporting group title	MenB+PCV Group
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Reporting group description:

Infant participants received rMenB+OMV NZ (Bexsero) along with PCV13 (Pevnar 13), Pediarix, Hiberix and Rotarix on Day 1 and Day 61 followed by rMenB+OMV NZ, PCV13, Pediarix and Hiberix on Day 121 and rMenB+OMV NZ, PCV13/PCV20, M-M-R II and Varivax on Day 301.

Reporting group title	Placebo+PCV Group
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Reporting group description:

Infant participants received PCV13 along with placebo, Pediarix, Hiberix and Rotarix on Day 1 and Day 61 followed by PCV13, Placebo, Pediarix and Hiberix on Day 121 and PCV13/PCV20, Placebo M-M-R II and Varivax on Day 301.

Serious adverse events	MenB+PCV Group	Placebo+PCV Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	35 / 781 (4.48%)	19 / 403 (4.71%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neuroblastoma			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Near drowning			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skull fracture			

subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Bronchogenic cyst			
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	2 / 781 (0.26%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile convulsion			
subjects affected / exposed	3 / 781 (0.38%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
PFAPA syndrome			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			

subjects affected / exposed	2 / 781 (0.26%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Lymphadenitis			
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Serum sickness			
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			

subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenoidal hypertrophy			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive sleep apnoea syndrome			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial hyperreactivity			
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillar hypertrophy			
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	3 / 781 (0.38%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			

subjects affected / exposed	2 / 781 (0.26%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Picornavirus infection			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 781 (0.26%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coxsackie viral infection			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complicated appendicitis			
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 781 (0.13%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			

subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			
subjects affected / exposed	4 / 781 (0.51%)	2 / 403 (0.50%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenovirus infection			
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	3 / 781 (0.38%)	2 / 403 (0.50%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus bronchitis			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	2 / 781 (0.26%)	2 / 403 (0.50%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection viral			
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinovirus infection			

subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 781 (0.13%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	1 / 781 (0.13%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 781 (0.13%)	1 / 403 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 1 diabetes mellitus			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	MenB+PCV Group	Placebo+PCV Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	771 / 781 (98.72%)	389 / 403 (96.53%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Haemangioma of skin			
subjects affected / exposed	1 / 781 (0.13%)	1 / 403 (0.25%)	
occurrences (all)	1	1	
Vascular disorders			
Scalp haematoma			
subjects affected / exposed	1 / 781 (0.13%)	1 / 403 (0.25%)	
occurrences (all)	1	1	
Cyanosis			
subjects affected / exposed	1 / 781 (0.13%)	1 / 403 (0.25%)	
occurrences (all)	1	1	
Flushing			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Lymphoedema			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Pallor			
subjects affected / exposed	3 / 781 (0.38%)	1 / 403 (0.25%)	
occurrences (all)	3	1	
General disorders and administration site conditions			
Injection site dryness			
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)	
occurrences (all)	0	1	
Administration site erythema			
subjects affected / exposed	460 / 781 (58.90%)	170 / 403 (42.18%)	
occurrences (all)	460	170	
Administration site induration			
subjects affected / exposed	480 / 781 (61.46%)	180 / 403 (44.67%)	
occurrences (all)	480	180	
Administration site pain			

subjects affected / exposed	582 / 781 (74.52%)	201 / 403 (49.88%)
occurrences (all)	582	201
Administration site swelling		
subjects affected / exposed	322 / 781 (41.23%)	122 / 403 (30.27%)
occurrences (all)	322	122
Adverse drug reaction		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Adverse food reaction		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Chills		
subjects affected / exposed	1 / 781 (0.13%)	1 / 403 (0.25%)
occurrences (all)	1	1
Crying		
subjects affected / exposed	432 / 781 (55.31%)	163 / 403 (40.45%)
occurrences (all)	433	163
Fatigue		
subjects affected / exposed	2 / 781 (0.26%)	2 / 403 (0.50%)
occurrences (all)	2	2
Hypothermia		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Induration		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Inflammation		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Influenza like illness		
subjects affected / exposed	3 / 781 (0.38%)	0 / 403 (0.00%)
occurrences (all)	3	0
Injection site bruising		
subjects affected / exposed	6 / 781 (0.77%)	6 / 403 (1.49%)
occurrences (all)	6	6
Injection site discolouration		

subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Injection site erythema		
subjects affected / exposed	2 / 781 (0.26%)	0 / 403 (0.00%)
occurrences (all)	2	0
Injection site laceration		
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)
occurrences (all)	0	1
Injection site nodule		
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)
occurrences (all)	0	1
Injection site rash		
subjects affected / exposed	2 / 781 (0.26%)	2 / 403 (0.50%)
occurrences (all)	2	6
Injection site reaction		
subjects affected / exposed	1 / 781 (0.13%)	1 / 403 (0.25%)
occurrences (all)	2	1
Injection site swelling		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Injection site urticaria		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	2	0
Injury associated with device		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Irritability postvaccinal		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Pain		
subjects affected / exposed	1 / 781 (0.13%)	1 / 403 (0.25%)
occurrences (all)	1	1
Peripheral swelling		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Pyrexia		

subjects affected / exposed	521 / 781 (66.71%)	172 / 403 (42.68%)	
occurrences (all)	543	184	
Swelling			
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)	
occurrences (all)	0	1	
Swelling face			
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)	
occurrences (all)	0	1	
Tenderness			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Vaccination site bruising			
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)	
occurrences (all)	0	1	
Vaccination site irritation			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Injection site induration			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Food allergy			
subjects affected / exposed	5 / 781 (0.64%)	2 / 403 (0.50%)	
occurrences (all)	5	2	
Seasonal allergy			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Social circumstances			
Child abuse			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			

Epididymal cyst			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Genital labial adhesions			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Genital rash			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Penile adhesion			
subjects affected / exposed	3 / 781 (0.38%)	0 / 403 (0.00%)	
occurrences (all)	4	0	
Penile cyst			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Penile dermatitis			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Vaginal discharge			
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Nasal congestion			
subjects affected / exposed	39 / 781 (4.99%)	17 / 403 (4.22%)	
occurrences (all)	44	19	
Asthma			
subjects affected / exposed	2 / 781 (0.26%)	0 / 403 (0.00%)	
occurrences (all)	2	0	
Brief resolved unexplained event			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Bronchial hyperreactivity			
subjects affected / exposed	1 / 781 (0.13%)	1 / 403 (0.25%)	
occurrences (all)	1	1	
Choking			

subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)
occurrences (all)	0	1
Cough		
subjects affected / exposed	51 / 781 (6.53%)	20 / 403 (4.96%)
occurrences (all)	58	25
Dysphonia		
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)
occurrences (all)	0	1
Epistaxis		
subjects affected / exposed	1 / 781 (0.13%)	1 / 403 (0.25%)
occurrences (all)	1	1
Hiccups		
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)
occurrences (all)	0	1
Oropharyngeal pain		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Respiratory disorder		
subjects affected / exposed	4 / 781 (0.51%)	3 / 403 (0.74%)
occurrences (all)	4	5
Respiratory symptom		
subjects affected / exposed	31 / 781 (3.97%)	17 / 403 (4.22%)
occurrences (all)	39	20
Rhinitis allergic		
subjects affected / exposed	3 / 781 (0.38%)	2 / 403 (0.50%)
occurrences (all)	4	2
Rhinorrhoea		
subjects affected / exposed	25 / 781 (3.20%)	12 / 403 (2.98%)
occurrences (all)	27	14
Sneezing		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Snoring		
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)
occurrences (all)	0	1
Upper respiratory tract irritation		

subjects affected / exposed occurrences (all)	0 / 781 (0.00%) 0	1 / 403 (0.25%) 1	
Wheezing subjects affected / exposed occurrences (all)	6 / 781 (0.77%) 6	5 / 403 (1.24%) 5	
Respiration abnormal subjects affected / exposed occurrences (all)	0 / 781 (0.00%) 0	1 / 403 (0.25%) 1	
Psychiatric disorders			
Breath holding subjects affected / exposed occurrences (all)	1 / 781 (0.13%) 1	0 / 403 (0.00%) 0	
Dependent personality disorder subjects affected / exposed occurrences (all)	1 / 781 (0.13%) 1	0 / 403 (0.00%) 0	
Emotional distress subjects affected / exposed occurrences (all)	1 / 781 (0.13%) 1	0 / 403 (0.00%) 0	
Insomnia subjects affected / exposed occurrences (all)	4 / 781 (0.51%) 4	5 / 403 (1.24%) 5	
Irritability subjects affected / exposed occurrences (all)	713 / 781 (91.29%) 738	330 / 403 (81.89%) 345	
Middle insomnia subjects affected / exposed occurrences (all)	0 / 781 (0.00%) 0	1 / 403 (0.25%) 1	
Selective eating disorder subjects affected / exposed occurrences (all)	1 / 781 (0.13%) 1	0 / 403 (0.00%) 0	
Sleep disorder subjects affected / exposed occurrences (all)	0 / 781 (0.00%) 0	1 / 403 (0.25%) 1	
Investigations			
Serum ferritin decreased			

subjects affected / exposed	1 / 781 (0.13%)	4 / 403 (0.99%)	
occurrences (all)	1	4	
Blood lead increased			
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)	
occurrences (all)	0	1	
Body temperature decreased			
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)	
occurrences (all)	0	1	
Body temperature increased			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Breath sounds abnormal			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Cardiac murmur			
subjects affected / exposed	2 / 781 (0.26%)	2 / 403 (0.50%)	
occurrences (all)	2	2	
Human rhinovirus test positive			
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)	
occurrences (all)	0	1	
Occult blood positive			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Platelet count increased			
subjects affected / exposed	1 / 781 (0.13%)	1 / 403 (0.25%)	
occurrences (all)	1	1	
SARS-CoV-2 test positive			
subjects affected / exposed	2 / 781 (0.26%)	2 / 403 (0.50%)	
occurrences (all)	2	2	
Weight decreased			
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)	
occurrences (all)	0	1	
White blood cell count decreased			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural			

complications			
Accidental exposure to product			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	2	0	
Accident at home			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Animal bite			
subjects affected / exposed	1 / 781 (0.13%)	1 / 403 (0.25%)	
occurrences (all)	1	1	
Arthropod bite			
subjects affected / exposed	2 / 781 (0.26%)	2 / 403 (0.50%)	
occurrences (all)	2	2	
Contusion			
subjects affected / exposed	5 / 781 (0.64%)	1 / 403 (0.25%)	
occurrences (all)	5	1	
Corneal abrasion			
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)	
occurrences (all)	0	1	
Craniocerebral injury			
subjects affected / exposed	3 / 781 (0.38%)	1 / 403 (0.25%)	
occurrences (all)	3	1	
Eyelid injury			
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)	
occurrences (all)	0	1	
Fall			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Foreign body ingestion			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Head injury			
subjects affected / exposed	4 / 781 (0.51%)	1 / 403 (0.25%)	
occurrences (all)	4	1	
Procedural pain			

subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)	
occurrences (all)	0	1	
Road traffic accident			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Scar			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Scrotal injury			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Skin laceration			
subjects affected / exposed	4 / 781 (0.51%)	0 / 403 (0.00%)	
occurrences (all)	4	0	
Superficial injury of eye			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Thermal burn			
subjects affected / exposed	1 / 781 (0.13%)	1 / 403 (0.25%)	
occurrences (all)	1	1	
Animal scratch			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Congenital, familial and genetic disorders			
Craniofacial deformity			
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)	
occurrences (all)	0	1	
Brachycephaly			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Dacryostenosis congenital			
subjects affected / exposed	1 / 781 (0.13%)	1 / 403 (0.25%)	
occurrences (all)	1	1	
Hydrocele			

subjects affected / exposed occurrences (all)	1 / 781 (0.13%) 1	0 / 403 (0.00%) 0	
Kidney duplex subjects affected / exposed occurrences (all)	1 / 781 (0.13%) 1	0 / 403 (0.00%) 0	
Macrocephaly subjects affected / exposed occurrences (all)	0 / 781 (0.00%) 0	1 / 403 (0.25%) 1	
Plagiocephaly subjects affected / exposed occurrences (all)	3 / 781 (0.38%) 3	3 / 403 (0.74%) 3	
Strabismus congenital subjects affected / exposed occurrences (all)	1 / 781 (0.13%) 1	0 / 403 (0.00%) 0	
Tethered oral tissue subjects affected / exposed occurrences (all)	1 / 781 (0.13%) 1	0 / 403 (0.00%) 0	
Developmental hip dysplasia subjects affected / exposed occurrences (all)	1 / 781 (0.13%) 1	0 / 403 (0.00%) 0	
Nervous system disorders			
Nystagmus subjects affected / exposed occurrences (all)	0 / 781 (0.00%) 0	1 / 403 (0.25%) 1	
Drizzling subjects affected / exposed occurrences (all)	0 / 781 (0.00%) 0	1 / 403 (0.25%) 1	
Fine motor delay subjects affected / exposed occurrences (all)	1 / 781 (0.13%) 1	0 / 403 (0.00%) 0	
Infant irritability subjects affected / exposed occurrences (all)	2 / 781 (0.26%) 2	2 / 403 (0.50%) 2	
Lethargy subjects affected / exposed occurrences (all)	1 / 781 (0.13%) 1	0 / 403 (0.00%) 0	

Movement disorder subjects affected / exposed occurrences (all)	1 / 781 (0.13%) 1	0 / 403 (0.00%) 0	
Myoclonus subjects affected / exposed occurrences (all)	0 / 781 (0.00%) 0	1 / 403 (0.25%) 1	
Petit mal epilepsy subjects affected / exposed occurrences (all)	0 / 781 (0.00%) 0	1 / 403 (0.25%) 1	
Speech disorder developmental subjects affected / exposed occurrences (all)	1 / 781 (0.13%) 1	1 / 403 (0.25%) 1	
Somnolence subjects affected / exposed occurrences (all)	681 / 781 (87.20%) 681	319 / 403 (79.16%) 322	
Blood and lymphatic system disorders			
Anaemia subjects affected / exposed occurrences (all)	3 / 781 (0.38%) 3	4 / 403 (0.99%) 4	
Iron deficiency anaemia subjects affected / exposed occurrences (all)	2 / 781 (0.26%) 2	0 / 403 (0.00%) 0	
Thrombocytosis subjects affected / exposed occurrences (all)	1 / 781 (0.13%) 1	0 / 403 (0.00%) 0	
Lymphadenopathy subjects affected / exposed occurrences (all)	20 / 781 (2.56%) 21	20 / 403 (4.96%) 23	
Ear and labyrinth disorders			
Cerumen impaction subjects affected / exposed occurrences (all)	1 / 781 (0.13%) 1	2 / 403 (0.50%) 2	
Conductive deafness subjects affected / exposed occurrences (all)	0 / 781 (0.00%) 0	1 / 403 (0.25%) 1	
Ear disorder			

subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)	
occurrences (all)	0	1	
Ear pain			
subjects affected / exposed	9 / 781 (1.15%)	5 / 403 (1.24%)	
occurrences (all)	9	5	
Eustachian tube dysfunction			
subjects affected / exposed	1 / 781 (0.13%)	1 / 403 (0.25%)	
occurrences (all)	1	1	
Middle ear effusion			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Otorrhoea			
subjects affected / exposed	2 / 781 (0.26%)	0 / 403 (0.00%)	
occurrences (all)	2	0	
Tympanic membrane perforation			
subjects affected / exposed	2 / 781 (0.26%)	0 / 403 (0.00%)	
occurrences (all)	2	0	
Eye disorders			
Eye movement disorder			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Astigmatism			
subjects affected / exposed	1 / 781 (0.13%)	1 / 403 (0.25%)	
occurrences (all)	1	1	
Dacryostenosis acquired			
subjects affected / exposed	3 / 781 (0.38%)	1 / 403 (0.25%)	
occurrences (all)	3	1	
Eczema eyelids			
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)	
occurrences (all)	0	1	
Eye discharge			
subjects affected / exposed	1 / 781 (0.13%)	3 / 403 (0.74%)	
occurrences (all)	1	3	
Eye swelling			
subjects affected / exposed	2 / 781 (0.26%)	1 / 403 (0.25%)	
occurrences (all)	2	2	

Eyelid rash			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Ocular hyperaemia			
subjects affected / exposed	1 / 781 (0.13%)	1 / 403 (0.25%)	
occurrences (all)	1	1	
Pseudostrabismus			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Scleral discolouration			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Swelling of eyelid			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Eyelid oedema			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Mucous stools			
subjects affected / exposed	2 / 781 (0.26%)	0 / 403 (0.00%)	
occurrences (all)	2	0	
Abdominal distension			
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)	
occurrences (all)	0	1	
Abdominal pain			
subjects affected / exposed	3 / 781 (0.38%)	0 / 403 (0.00%)	
occurrences (all)	3	0	
Abnormal faeces			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Anal fissure			
subjects affected / exposed	1 / 781 (0.13%)	2 / 403 (0.50%)	
occurrences (all)	1	2	
Aphthous ulcer			

subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)
occurrences (all)	0	1
Constipation		
subjects affected / exposed	31 / 781 (3.97%)	12 / 403 (2.98%)
occurrences (all)	32	13
Diarrhoea		
subjects affected / exposed	334 / 781 (42.77%)	178 / 403 (44.17%)
occurrences (all)	350	193
Dysphagia		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Faeces discoloured		
subjects affected / exposed	2 / 781 (0.26%)	1 / 403 (0.25%)
occurrences (all)	2	1
Faeces hard		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Flatulence		
subjects affected / exposed	4 / 781 (0.51%)	1 / 403 (0.25%)
occurrences (all)	4	1
Food protein-induced enterocolitis syndrome		
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)
occurrences (all)	0	1
Frequent bowel movements		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Gastrooesophageal reflux disease		
subjects affected / exposed	14 / 781 (1.79%)	9 / 403 (2.23%)
occurrences (all)	14	9
Gastrooesophageal reflux in neonate		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Gingival cyst		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0

Gingival disorder		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Haematochezia		
subjects affected / exposed	5 / 781 (0.64%)	1 / 403 (0.25%)
occurrences (all)	5	1
Infantile colic		
subjects affected / exposed	0 / 781 (0.00%)	2 / 403 (0.50%)
occurrences (all)	0	2
Infantile spitting up		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Oral mucosal eruption		
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)
occurrences (all)	0	1
Protein-losing gastroenteropathy		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Regurgitation		
subjects affected / exposed	1 / 781 (0.13%)	1 / 403 (0.25%)
occurrences (all)	1	1
Retching		
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)
occurrences (all)	0	1
Stomatitis		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Teething		
subjects affected / exposed	75 / 781 (9.60%)	46 / 403 (11.41%)
occurrences (all)	84	55
Toothache		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Vomiting		
subjects affected / exposed	317 / 781 (40.59%)	159 / 403 (39.45%)
occurrences (all)	328	174

Vomiting projectile subjects affected / exposed occurrences (all)	1 / 781 (0.13%) 1	1 / 403 (0.25%) 1	
Post-tussive vomiting subjects affected / exposed occurrences (all)	1 / 781 (0.13%) 1	1 / 403 (0.25%) 1	
Skin and subcutaneous tissue disorders			
Post inflammatory pigmentation change subjects affected / exposed occurrences (all)	1 / 781 (0.13%) 1	0 / 403 (0.00%) 0	
Acne subjects affected / exposed occurrences (all)	0 / 781 (0.00%) 0	1 / 403 (0.25%) 1	
Acne infantile subjects affected / exposed occurrences (all)	2 / 781 (0.26%) 2	0 / 403 (0.00%) 0	
Blood blister subjects affected / exposed occurrences (all)	1 / 781 (0.13%) 1	0 / 403 (0.00%) 0	
Dermatitis subjects affected / exposed occurrences (all)	9 / 781 (1.15%) 9	2 / 403 (0.50%) 2	
Dermatitis atopic subjects affected / exposed occurrences (all)	8 / 781 (1.02%) 8	3 / 403 (0.74%) 3	
Dermatitis contact subjects affected / exposed occurrences (all)	4 / 781 (0.51%) 4	1 / 403 (0.25%) 1	
Dermatitis diaper subjects affected / exposed occurrences (all)	38 / 781 (4.87%) 41	22 / 403 (5.46%) 25	
Dry skin subjects affected / exposed occurrences (all)	4 / 781 (0.51%) 4	4 / 403 (0.99%) 4	
Ecchymosis			

subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Eczema		
subjects affected / exposed	16 / 781 (2.05%)	10 / 403 (2.48%)
occurrences (all)	16	10
Eczema infantile		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Erythema		
subjects affected / exposed	7 / 781 (0.90%)	1 / 403 (0.25%)
occurrences (all)	7	1
Ingrowing nail		
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)
occurrences (all)	0	1
Intertrigo		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Miliaria		
subjects affected / exposed	1 / 781 (0.13%)	3 / 403 (0.74%)
occurrences (all)	1	3
Palmar-plantar erythrodysaesthesia syndrome		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Perioral dermatitis		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Pruritus		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Rash erythematous		
subjects affected / exposed	2 / 781 (0.26%)	0 / 403 (0.00%)
occurrences (all)	2	0
Rash macular		
subjects affected / exposed	2 / 781 (0.26%)	1 / 403 (0.25%)
occurrences (all)	2	1

Rash maculo-papular subjects affected / exposed occurrences (all)	1 / 781 (0.13%) 1	0 / 403 (0.00%) 0	
Rash papular subjects affected / exposed occurrences (all)	0 / 781 (0.00%) 0	1 / 403 (0.25%) 1	
Seborrhoea subjects affected / exposed occurrences (all)	1 / 781 (0.13%) 1	1 / 403 (0.25%) 1	
Seborrhoeic dermatitis subjects affected / exposed occurrences (all)	3 / 781 (0.38%) 3	4 / 403 (0.99%) 4	
Skin discolouration subjects affected / exposed occurrences (all)	1 / 781 (0.13%) 1	0 / 403 (0.00%) 0	
Skin exfoliation subjects affected / exposed occurrences (all)	1 / 781 (0.13%) 1	0 / 403 (0.00%) 0	
Skin fissures subjects affected / exposed occurrences (all)	1 / 781 (0.13%) 1	0 / 403 (0.00%) 0	
Skin irritation subjects affected / exposed occurrences (all)	2 / 781 (0.26%) 2	0 / 403 (0.00%) 0	
Umbilical erythema subjects affected / exposed occurrences (all)	1 / 781 (0.13%) 1	0 / 403 (0.00%) 0	
Urticaria subjects affected / exposed occurrences (all)	5 / 781 (0.64%) 5	3 / 403 (0.74%) 4	
Rash subjects affected / exposed occurrences (all)	216 / 781 (27.66%) 224	106 / 403 (26.30%) 117	
Renal and urinary disorders Renal hypertrophy			

subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Single functional kidney			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Acquired plagiocephaly			
subjects affected / exposed	2 / 781 (0.26%)	1 / 403 (0.25%)	
occurrences (all)	2	1	
Arthralgia			
subjects affected / exposed	2 / 781 (0.26%)	0 / 403 (0.00%)	
occurrences (all)	2	0	
Jaw clicking			
subjects affected / exposed	2 / 781 (0.26%)	0 / 403 (0.00%)	
occurrences (all)	2	0	
Joint noise			
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)	
occurrences (all)	0	1	
Muscle tightness			
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)	
occurrences (all)	0	1	
Muscular weakness			
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)	
occurrences (all)	0	1	
Musculoskeletal stiffness			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Pain in extremity			
subjects affected / exposed	2 / 781 (0.26%)	0 / 403 (0.00%)	
occurrences (all)	3	0	
Torticollis			
subjects affected / exposed	3 / 781 (0.38%)	2 / 403 (0.50%)	
occurrences (all)	3	2	
Infections and infestations			

Acute sinusitis		
subjects affected / exposed	2 / 781 (0.26%)	1 / 403 (0.25%)
occurrences (all)	3	2
Abscess limb		
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)
occurrences (all)	0	1
Body tinea		
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)
occurrences (all)	0	1
Influenza		
subjects affected / exposed	13 / 781 (1.66%)	3 / 403 (0.74%)
occurrences (all)	13	3
Bronchitis		
subjects affected / exposed	3 / 781 (0.38%)	1 / 403 (0.25%)
occurrences (all)	3	1
Bullous impetigo		
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)
occurrences (all)	0	1
COVID-19		
subjects affected / exposed	6 / 781 (0.77%)	5 / 403 (1.24%)
occurrences (all)	6	5
Candida infection		
subjects affected / exposed	5 / 781 (0.64%)	0 / 403 (0.00%)
occurrences (all)	5	0
Candida nappy rash		
subjects affected / exposed	10 / 781 (1.28%)	3 / 403 (0.74%)
occurrences (all)	11	3
Cellulitis		
subjects affected / exposed	2 / 781 (0.26%)	2 / 403 (0.50%)
occurrences (all)	2	2
Chronic sinusitis		
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)
occurrences (all)	0	1
Conjunctivitis		
subjects affected / exposed	17 / 781 (2.18%)	15 / 403 (3.72%)
occurrences (all)	20	17

Conjunctivitis bacterial subjects affected / exposed occurrences (all)	4 / 781 (0.51%) 4	0 / 403 (0.00%) 0
Conjunctivitis viral subjects affected / exposed occurrences (all)	0 / 781 (0.00%) 0	1 / 403 (0.25%) 1
Coxsackie viral infection subjects affected / exposed occurrences (all)	2 / 781 (0.26%) 2	1 / 403 (0.25%) 1
Croup infectious subjects affected / exposed occurrences (all)	24 / 781 (3.07%) 25	3 / 403 (0.74%) 4
Cystitis subjects affected / exposed occurrences (all)	1 / 781 (0.13%) 1	0 / 403 (0.00%) 0
Dacryocystitis subjects affected / exposed occurrences (all)	1 / 781 (0.13%) 1	0 / 403 (0.00%) 0
Ear infection subjects affected / exposed occurrences (all)	4 / 781 (0.51%) 4	0 / 403 (0.00%) 0
Erythema infectiosum subjects affected / exposed occurrences (all)	2 / 781 (0.26%) 2	0 / 403 (0.00%) 0
Exanthema subitum subjects affected / exposed occurrences (all)	2 / 781 (0.26%) 2	0 / 403 (0.00%) 0
Eye infection subjects affected / exposed occurrences (all)	0 / 781 (0.00%) 0	1 / 403 (0.25%) 2
Folliculitis subjects affected / exposed occurrences (all)	0 / 781 (0.00%) 0	1 / 403 (0.25%) 1
Fungal skin infection subjects affected / exposed occurrences (all)	3 / 781 (0.38%) 3	0 / 403 (0.00%) 0

Gastroenteritis		
subjects affected / exposed	8 / 781 (1.02%)	5 / 403 (1.24%)
occurrences (all)	8	5
Gastroenteritis viral		
subjects affected / exposed	9 / 781 (1.15%)	1 / 403 (0.25%)
occurrences (all)	9	1
Gastrointestinal viral infection		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Hand-foot-and-mouth disease		
subjects affected / exposed	7 / 781 (0.90%)	3 / 403 (0.74%)
occurrences (all)	7	3
Impetigo		
subjects affected / exposed	3 / 781 (0.38%)	3 / 403 (0.74%)
occurrences (all)	4	3
Bronchiolitis		
subjects affected / exposed	30 / 781 (3.84%)	13 / 403 (3.23%)
occurrences (all)	31	16
Injection site cellulitis		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Laryngotracheitis obstructive		
subjects affected / exposed	2 / 781 (0.26%)	2 / 403 (0.50%)
occurrences (all)	2	2
Nail infection		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Nasopharyngitis		
subjects affected / exposed	40 / 781 (5.12%)	18 / 403 (4.47%)
occurrences (all)	46	20
Onychomycosis		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Oral candidiasis		
subjects affected / exposed	5 / 781 (0.64%)	4 / 403 (0.99%)
occurrences (all)	5	4

Oral viral infection		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Otitis externa		
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)
occurrences (all)	0	1
Otitis media		
subjects affected / exposed	47 / 781 (6.02%)	29 / 403 (7.20%)
occurrences (all)	55	37
Otitis media acute		
subjects affected / exposed	33 / 781 (4.23%)	23 / 403 (5.71%)
occurrences (all)	42	28
Otitis media chronic		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Parainfluenzae virus infection		
subjects affected / exposed	2 / 781 (0.26%)	0 / 403 (0.00%)
occurrences (all)	2	0
Paronychia		
subjects affected / exposed	1 / 781 (0.13%)	1 / 403 (0.25%)
occurrences (all)	1	1
Parvovirus infection		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Periorbital cellulitis		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Pertussis		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Pharyngitis		
subjects affected / exposed	5 / 781 (0.64%)	1 / 403 (0.25%)
occurrences (all)	5	1
Pharyngitis streptococcal		
subjects affected / exposed	3 / 781 (0.38%)	0 / 403 (0.00%)
occurrences (all)	3	0

Pneumonia		
subjects affected / exposed	2 / 781 (0.26%)	1 / 403 (0.25%)
occurrences (all)	2	1
Pustule		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Respiratory syncytial virus bronchiolitis		
subjects affected / exposed	3 / 781 (0.38%)	3 / 403 (0.74%)
occurrences (all)	3	3
Respiratory syncytial virus infection		
subjects affected / exposed	9 / 781 (1.15%)	3 / 403 (0.74%)
occurrences (all)	9	3
Respiratory tract infection viral		
subjects affected / exposed	2 / 781 (0.26%)	1 / 403 (0.25%)
occurrences (all)	2	1
Rhinitis		
subjects affected / exposed	5 / 781 (0.64%)	0 / 403 (0.00%)
occurrences (all)	5	0
Roseola		
subjects affected / exposed	2 / 781 (0.26%)	1 / 403 (0.25%)
occurrences (all)	2	1
Rotavirus infection		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Sinusitis		
subjects affected / exposed	6 / 781 (0.77%)	6 / 403 (1.49%)
occurrences (all)	6	6
Skin candida		
subjects affected / exposed	5 / 781 (0.64%)	3 / 403 (0.74%)
occurrences (all)	5	3
Skin infection		
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)
occurrences (all)	1	0
Suspected COVID-19		

subjects affected / exposed	4 / 781 (0.51%)	1 / 403 (0.25%)	
occurrences (all)	4	1	
Tinea cruris			
subjects affected / exposed	1 / 781 (0.13%)	1 / 403 (0.25%)	
occurrences (all)	1	1	
Upper respiratory tract infection			
subjects affected / exposed	125 / 781 (16.01%)	62 / 403 (15.38%)	
occurrences (all)	149	79	
Urinary tract infection			
subjects affected / exposed	4 / 781 (0.51%)	2 / 403 (0.50%)	
occurrences (all)	4	2	
Viral infection			
subjects affected / exposed	13 / 781 (1.66%)	7 / 403 (1.74%)	
occurrences (all)	14	7	
Viral pharyngitis			
subjects affected / exposed	3 / 781 (0.38%)	1 / 403 (0.25%)	
occurrences (all)	3	1	
Viral rash			
subjects affected / exposed	3 / 781 (0.38%)	1 / 403 (0.25%)	
occurrences (all)	3	1	
Viral upper respiratory tract infection			
subjects affected / exposed	16 / 781 (2.05%)	12 / 403 (2.98%)	
occurrences (all)	17	12	
Wound infection			
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)	
occurrences (all)	0	1	
Respiratory tract infection			
subjects affected / exposed	1 / 781 (0.13%)	2 / 403 (0.50%)	
occurrences (all)	1	2	
Metabolism and nutrition disorders			
Breast milk substitute intolerance			
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)	
occurrences (all)	0	1	
Decreased appetite			
subjects affected / exposed	4 / 781 (0.51%)	2 / 403 (0.50%)	
occurrences (all)	4	2	

Feeding disorder			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Food intolerance			
subjects affected / exposed	1 / 781 (0.13%)	0 / 403 (0.00%)	
occurrences (all)	1	0	
Hypophagia			
subjects affected / exposed	543 / 781 (69.53%)	216 / 403 (53.60%)	
occurrences (all)	544	217	
Iron deficiency			
subjects affected / exposed	3 / 781 (0.38%)	1 / 403 (0.25%)	
occurrences (all)	3	1	
Milk soy protein intolerance			
subjects affected / exposed	0 / 781 (0.00%)	1 / 403 (0.25%)	
occurrences (all)	0	1	
Weight gain poor			
subjects affected / exposed	3 / 781 (0.38%)	0 / 403 (0.00%)	
occurrences (all)	3	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 November 2018	The protocol was amended to revise the endpoints and success criteria based on using the strain M10713, for evaluating immune responses to the NHBA antigen.
10 April 2020	The protocol was amended to outline measures that were applicable during special circumstances (e.g., COVID-19 pandemic). The purpose of the amendment was to protect subject's welfare, and ensure the potential benefit to the subject and promote data integrity.
09 December 2021	The protocol was amended to update the criteria for the primary and key secondary immunogenicity objectives and the total number of enrolled subjects was revised to 1200.
24 October 2022	The protocol was amended to shorten the safety follow-up period to 6 months in subjects who had not reached the 6-month safety follow-up after the last dose, at the time this amendment took effect.
19 December 2023	The protocol was amended to align with the update of CDC's ACIP for the US NIP (National Immunization Program). According to this ACIP update, the 20-valent pneumococcal conjugate vaccine (PCV20) was listed as one of the recommended vaccines for the immunization of pneumococcal disease in children in U.S while PCV13 was no longer recommended for full series of pneumococcal vaccination. Children who received 3 PCV13 doses before 12 months but had not received their fourth booster dose, had the option to receive PCV20 or PCV13. Therefore, to incorporate the ACIP recommendations, subjects who had not reached their visit 5 at the time when this protocol amendment became effective had the option to receive either PCV13 or PCV20 based on the investigator judgment and/or parent's preference.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported