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	v1
This version publication date	13 March 2026
First version publication date	13 March 2026

Trial information

Trial identification

Sponsor protocol code	205239

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 (Prevnar 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	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	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 (Prevnar 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 (Prevnar 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, Prevnar 13	100	39		
Erythema, Placebo	0	25		
Erythema, Pediarix	72	32		
Erythema, Hiberix	74	17		
Induration, Bexsero	204	0		
Induration, Prevnar 13	127	67		
Induration, Placebo	0	22		
Induration, Pediarix	70	34		
Induration, Hiberix	77	20		
Swelling, Bexsero	132	0		
Swelling, Prevnar 13	77	34		
Swelling, Placebo	0	21		
Swelling, Pediarix	53	21		

Swelling, Hiberix	54	12		
Tenderness, Bexsero	352	0		
Tenderness, Prevnar 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]

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 (≥)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

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

	site events after the second vaccination administered at Day

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

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]

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]

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 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]

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 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 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[8]

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

End point timeframe:

Day 301 to Day 330

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	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 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[9]

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 301 to Day 307

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	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 reporting any unsolicted AEs after the third vaccination administered at Day 121

End point title	Number of participants reporting any unsolicted AEs after the third vaccination administered at Day 121[10]

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

End point timeframe:

Day 121 to Day 150

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	725	374		
Units: Participants	230	120		

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]

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

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	375	177		

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[12]

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

End point timeframe:

Day 1 to Day 30

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	775	401		
Units: Participants	214	103		

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[13]

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

End point timeframe:

Day 61 to Day 90

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	745	388		
Units: Participants	225	119		

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[14]

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

End point timeframe:

Day 301 to Day 330

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	668	339		
Units: Participants	248	144		

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with human serum bactericidal assay (hSBA) antibody titers >= 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 >= 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]

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 ≥ LLOQ is ≥ 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

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 >= LLOQ against all serogroup B test strains combined (composite response)

End point title	Percentage of participants with hSBA titers >= LLOQ against all serogroup B test strains combined (composite response)[17][18]

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 ≥ 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 ≥ LLOQ is ≥ 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

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]

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 ≥ 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 ≥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

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

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 ≥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

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 Immunoglobubin (IgG) Antibodies Against 13 PCV13 Antigens at 1 Month After Third Vaccination

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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 >= 0.35 µg/mL

End point title	Percentage of participants with serum pneumococcal anti-capsular polysaccharide IgG >= 0.35 µg/mL

End point description:

The immune response to PCV13 is evaluated by measuring the percentage of participants with serum IgG concentrations ≥ 0.35 µg/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

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

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

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

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

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

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

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

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

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

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

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

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

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	-0.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.43
upper limit	1.87

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	-0.09
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

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

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	0.63
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	0.73

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 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 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 antibodies concentrations against hepatitis B surface antigen (AntiHBsAg) >= 10 mIU/mL

End point title	Percentage of participants with antibodies concentrations against hepatitis B surface antigen (AntiHBsAg) >= 10 mIU/mL

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

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-polyribosyl-ribitol phosphate (PRP) concentration >= 0.15 µg/mL and >= 1 µg/mL

End point title	Percentage of participants with anti-polyribosyl-ribitol phosphate (PRP) concentration >= 0.15 µg/mL and >= 1 µg/mL

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

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%)				
>= 0.15 µg/mL	98.3 (96.3 to 99.4)	97.7 (95.1 to 99.2)		
>= 1 µg/mL	87.0 (83.0 to 90.4)	84.1 (79.1 to 88.3)		

Statistical analyses

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	2.94
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.63
upper limit	8.78

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-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-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: 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]

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

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: 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: 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: 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]

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

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]

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

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]

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

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]

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

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 >= 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 >= LLOQ for each of the Serogroup B test strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA P1.4), and M13520 (NHBA)[28]

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

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

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

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: 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: 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]

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 >= LLOQ, whichever is greater; - if pre-vaccination titer is >= LOD but <LLOQ, then a post-vaccination titer >= 4 times the LLOQ; - if pre-vaccination titer is >= 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

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: 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: 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

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	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 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: 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

End point description:

Seroresponse is defined as post-vaccination anti-VZV virus, anti-measles virus, anti-mumps virus and anti-rubella virus antibody concentration >= 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

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

Dictionary used

Dictionary name	MedDRA
Dictionary version	27.1

Reporting groups

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 title	MenB+PCV Group

Reporting group description:

Infant participants received rMenB+OMV NZ (Bexsero) along with PCV13 (Prevnar 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.

Serious adverse events	Placebo+PCV Group	MenB+PCV Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	19 / 403 (4.71%)	35 / 781 (4.48%)	
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	0 / 403 (0.00%)	1 / 781 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Near drowning			
subjects affected / exposed	0 / 403 (0.00%)	1 / 781 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skull fracture			

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

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

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

subjects affected / exposed	1 / 403 (0.25%)	2 / 781 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 403 (0.25%)	0 / 781 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Picornavirus infection			
subjects affected / exposed	0 / 403 (0.00%)	1 / 781 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 403 (0.25%)	2 / 781 (0.26%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coxsackie viral infection			
subjects affected / exposed	0 / 403 (0.00%)	1 / 781 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complicated appendicitis			
subjects affected / exposed	1 / 403 (0.25%)	0 / 781 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	0 / 403 (0.00%)	1 / 781 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 403 (0.25%)	1 / 781 (0.13%)	
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	0 / 403 (0.00%)	1 / 781 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			
subjects affected / exposed	2 / 403 (0.50%)	4 / 781 (0.51%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenovirus infection			
subjects affected / exposed	1 / 403 (0.25%)	0 / 781 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	0 / 403 (0.00%)	1 / 781 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	2 / 403 (0.50%)	3 / 781 (0.38%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus bronchitis			
subjects affected / exposed	0 / 403 (0.00%)	1 / 781 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	2 / 403 (0.50%)	2 / 781 (0.26%)	
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	1 / 403 (0.25%)	0 / 781 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinovirus infection			

subjects affected / exposed	0 / 403 (0.00%)	1 / 781 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	0 / 403 (0.00%)	1 / 781 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 403 (0.25%)	0 / 781 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 403 (0.25%)	1 / 781 (0.13%)	
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 / 403 (0.25%)	1 / 781 (0.13%)	
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 / 403 (0.25%)	1 / 781 (0.13%)	
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	0 / 403 (0.00%)	1 / 781 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 403 (0.00%)	1 / 781 (0.13%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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