Clinical trial results:
Immunogenicity and Safety Study of an Investigational Quadrivalent Meningococcal Conjugate Vaccine when Administered Concomitantly with Routine Pediatric Vaccines in Healthy Infants and Toddlers

Summary

EudraCT number	2018-001473-24
Trial protocol	Outside EU/EEA
Global end of trial date	22 September 2023

Results information

Result version number	v1 (current)
This version publication date	14 July 2024
First version publication date	14 July 2024

Trial information

Trial identification

Sponsor protocol code	MET42

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03537508
WHO universal trial number (UTN)	U1111-1183-6361
Other trial identifiers	BB-IND: 14171

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur Inc.
Sponsor organisation address	Discovery Drive, Swiftwater, PA, United States, 18370-0187
Public contact	Trial Transparency Team, Sanofi Pasteur, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi Pasteur, Contact-US@sanofi.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001930-PIP01-16
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	08 March 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 September 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

-To demonstrate the non-inferiority (NI) of the serum bactericidal assay using human complement (hSBA) vaccine seroresponse to meningococcal serogroups A, C, Y, and W following the administration of a 4-dose series of meningococcal polysaccharide (serogroups A, C, Y, and W) tetanus toxoid conjugate vaccine (MenACYW conjugate vaccine) compared to a 4-dose series of meningococcal (groups A, C, Y, and W-135) oligosaccharide diphtheria cross reacting material (CRM) 197 conjugate vaccine (MENVEO®) when given concomitantly with routine pediatric vaccines to infants and toddlers 6 weeks old to 15 months old.
-To demonstrate the NI of the hSBA antibody response to meningococcal serogroups A, C, Y, and W following the administration of 3 doses in infancy of MenACYW conjugate vaccine compared to 3 doses in infancy of MENVEO when given concomitantly with routine pediatric vaccines to infants at 2, 4, and 6 months of age.

Protection of trial subjects:

Vaccinations were performed by qualified and trained study personnel. Participants with allergy to any of the vaccine components were not vaccinated. After vaccination, participants were also kept under clinical observation for 30 minutes to ensure their safety. Appropriate medical equipment were also available on site in case of any immediate allergic reactions.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 April 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Puerto Rico: 380
Country: Number of subjects enrolled	United States: 2247
Worldwide total number of subjects	2627
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)	2627
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:

The study was conducted at 69 investigational sites in Puerto Rico and the United States. Healthy infants aged greater than or equal to (>=)42 to less than or equal to (<=)89 days were randomized in a 2:1 ratio to either Group 1: MenACYW conjugate vaccine and routine pediatric vaccines or Group 2: MENVEO and routine pediatric vaccines.

Pre-assignment

Screening details:

Each group was further randomized in a 2:1 ratio in 2 subgroups based on the time of analyses conducted in the 2nd year of life (30 days after the 12-month vaccinations [Groups 1a and 2a] or 30 days after the 15-month vaccinations [Groups 1b and 2b], respectively. A total of 2627 participants were enrolled in this 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, Carer, Data analyst, Assessor, Subject

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1: MenACYW conjugate vaccine

Arm description:

Group 1 was further randomized as Groups 1a and 1b based on the 4th dose timing, i.e. 12 to 15 months and 15 to 18 months respectively. Participants received MenACYW conjugate vaccine 0.5 milliliter (mL) as an intramuscular (IM) injection at 2, 4, 6, and 12 to 15 (Group 1a)/15-18 (Group 1b) months of age along with Pentacel® (diphtheria-tetanus-acellular pertussis [DTaP-IPV/Hib] vaccine) at 2, 4, 6 and 15 to 18 months of age; PREVNAR 13® (pneumococcal 13-valent conjugate vaccine [PCV13] at 2, 4, 6, and 12 to 15 months of age; RotaTeq® (pentavalent rotavirus vaccine [RV5]) at 2, 4, and 6 months of age; ENGERIX-B® (hepatitis B vaccine) at 2 and 6 months of age; M-M-R® II (measles, mumps, and rubella vaccine) and VARIVAX® (varicella vaccine) at 12 to 15 months of age. In addition to the above, Group 1b participants also received first dose of HAVRIX® (hepatitis A vaccine) at 15 to 18 months of age as a part of the study.

Arm type	Experimental
Investigational medicinal product name	Meningococcal Polysaccharide (Serogroups A, C, Y, and W) Tetanus Toxoid Conjugate Vaccine
Investigational medicinal product code	
Other name	MenACYW conjugate vaccine
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants received MenACYW conjugate vaccine
at 2, 4, 6, and 12 to 15 (Group 1a)/15-18 (Group 1b) months of age.

Investigational medicinal product name	Diphtheria and Tetanus Toxoids and Acellular Pertussis Poliovirus and Hemophilus b Conjugate Vaccine
Investigational medicinal product code	
Other name	Pentacel
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants received Pentacel vaccine at 2, 4, 6, 15 to 18 months of age.

Investigational medicinal product name	Pneumococcal 13-valent Conjugate Vaccine
Investigational medicinal product code	
Other name	PREVNAR 13, PCV13
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants received PREVNAR 13 vaccine at 2, 4, 6, and 12 to 15 months of age.

Investigational medicinal product name	Rotavirus Vaccine
Investigational medicinal product code	
Other name	RotaTeq
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Participants received RotaTeq vaccine at 2, 4, and 6 months of age.

Investigational medicinal product name	Hepatitis B Vaccine
Investigational medicinal product code	
Other name	ENGERIX-B
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants received ENGERIX-B vaccine at 2 and 6 months of age.

Investigational medicinal product name	Measles, Mumps, and Rubella Virus Vaccine
Investigational medicinal product code	
Other name	M-M-R II
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received M-M-R II vaccine at 12 to 15 months of age.

Investigational medicinal product name	Varicella Virus Vaccine
Investigational medicinal product code	
Other name	VARIVAX
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants received VARIVAX vaccine at 12 to 15 months of age.

Investigational medicinal product name	Hepatitis A vaccine
Investigational medicinal product code	
Other name	HAVRIX
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants in Group 1b received HAVRIX vaccine at 15 to 18 months of age as a part of this study. For Group 1a, it was administered after last study visit as per standard guidelines.

Arm title	Group 2: MENVEO

Arm description:

Group 2 was further randomized as Groups 2a and 2b based on the timing of blood collection, i.e. 12 and 15 months respectively. Participants received MENVEO conjugate vaccine 0.5 mL as an IM injection at 2, 4, 6, and 12 months of age along with Pentacel (DTaP-IPV/Hib vaccine) at 2, 4, 6 and 15 to 18 months of age; PREVNAR 13 (PCV13) at 2, 4, 6, and 12 months of age; RotaTeq (rotavirus vaccine) at 2, 4, and 6 months of age; ENGERIX-B (hepatitis B vaccine) at 2 and 6 months of age; M-M-R II (measles, mumps, and rubella vaccine) and VARIVAX (varicella vaccine) at 12 months of age. In addition, they also received first dose of HAVRIX (hepatitis A vaccine) at 15 to 18 months of age.

Arm type	Experimental
Investigational medicinal product name	Meningococcal (Groups A, C, Y and W 135) Oligosaccharide Diphtheria CRM197 Conjugate Vaccine
Investigational medicinal product code	
Other name	MENVEO
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intramuscular use
Dosage and administration details: Participants received MENVEO vaccine at 2, 4, 6, and 12 months of age.	
Investigational medicinal product name	Diphtheria and Tetanus Toxoids and Acellular Pertussis Poliovirus and Hemophilus b Conjugate Vaccine
Investigational medicinal product code	
Other name	Pentacel
Pharmaceutical forms	Concentrate and solvent for solution for injection
Routes of administration	Intramuscular use
Dosage and administration details: Participants received Pentacel vaccine at 2, 4, 6 and 15 to 18 months of age.	
Investigational medicinal product name	Varicella Virus Vaccine
Investigational medicinal product code	
Other name	VARIVAX
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use
Dosage and administration details: Participants received VARIVAX vaccine at 12 months of age.	
Investigational medicinal product name	Rotavirus Vaccine
Investigational medicinal product code	
Other name	RotaTeq
Pharmaceutical forms	Oral solution
Routes of administration	Oral use
Dosage and administration details: Participants received RotaTeq vaccine at 2, 4, and 6 months of age.	
Investigational medicinal product name	Hepatitis B Vaccine
Investigational medicinal product code	
Other name	ENGERIX-B
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details: Participants received ENGERIX-B vaccine at 2 and 6 months of age.	
Investigational medicinal product name	Measles, Mumps, and Rubella Virus Vaccine
Investigational medicinal product code	
Other name	M-M-R II
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use
Dosage and administration details: Participants received M-M-R II vaccine at 12 months of age.	
Investigational medicinal product name	Hepatitis A vaccine
Investigational medicinal product code	
Other name	HAVRIX
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use
Dosage and administration details: Participants received HAVRIX vaccine at 15 to 18 months of age.	

Investigational medicinal product name	Pneumococcal 13-valent Conjugate Vaccine
Investigational medicinal product code	
Other name	PREVNAR 13, PCV13
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants received PREVNAR 13 vaccine at 2, 4, 6, and 12 months of age.

Number of subjects in period 1	Group 1: MenACYW conjugate vaccine	Group 2: MENVEO
Started	1746	881
Safety analysis set (SafAS)	1727	867
Vaccinated at 2 months	1727	869
Vaccinated at 4 months	1619	828
Vaccinated at 6 months	1543	793
Vaccinated at 12 months	1411	708
Vaccinated at 15 months	445 [1]	644
Completed	1330	623
Not completed	416	258
Adverse event, non-fatal	2	1
Lost to follow-up	86	60
Withdrawal by parent/guardian	263	149
Protocol deviation	65	48

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Only Group 1b participants were vaccinated

Baseline characteristics

Reporting groups	
Reporting group title	Group 1: MenACYW conjugate vaccine

Reporting group description:

Group 1 was further randomized as Groups 1a and 1b based on the 4th dose timing, i.e. 12 to 15 months and 15 to 18 months respectively. Participants received MenACYW conjugate vaccine 0.5 milliliter (mL) as an intramuscular (IM) injection at 2, 4, 6, and 12 to 15 (Group 1a)/15-18 (Group 1b) months of age along with Pentacel® (diphtheria-tetanus-acellular pertussis [DTaP-IPV/Hib] vaccine) at 2, 4, 6 and 15 to 18 months of age; PREVNAR 13® (pneumococcal 13-valent conjugate vaccine [PCV13] at 2, 4, 6, and 12 to 15 months of age; RotaTeq® (pentavalent rotavirus vaccine [RV5]) at 2, 4, and 6 months of age; ENGERIX-B® (hepatitis B vaccine) at 2 and 6 months of age; M-M-R® II (measles, mumps, and rubella vaccine) and VARIVAX® (varicella vaccine) at 12 to 15 months of age. In addition to the above, Group 1b participants also received first dose of HAVRIX® (hepatitis A vaccine) at 15 to 18 months of age as a part of the study.

Reporting group title	Group 2: MENVEO

Reporting group description:

Group 2 was further randomized as Groups 2a and 2b based on the timing of blood collection, i.e. 12 and 15 months respectively. Participants received MENVEO conjugate vaccine 0.5 mL as an IM injection at 2, 4, 6, and 12 months of age along with Pentacel (DTaP-IPV/Hib vaccine) at 2, 4, 6 and 15 to 18 months of age; PREVNAR 13 (PCV13) at 2, 4, 6, and 12 months of age; RotaTeq (rotavirus vaccine) at 2, 4, and 6 months of age; ENGERIX-B (hepatitis B vaccine) at 2 and 6 months of age; M-M-R II (measles, mumps, and rubella vaccine) and VARIVAX (varicella vaccine) at 12 months of age. In addition, they also received first dose of HAVRIX (hepatitis A vaccine) at 15 to 18 months of age.

Reporting group values	Group 1: MenACYW conjugate vaccine	Group 2: MENVEO	Total
Number of subjects	1746	881	2627
Age Categorical Units: Subjects			
Age Continuous Units: days			
arithmetic mean	65.3	65.3	
standard deviation	± 8.02	± 7.81	-
Gender Categorical Units: Subjects			
Female	828	415	1243
Male	918	466	1384
Race Units: Subjects			
American Indian or Alaska Native	11	3	14
Asian	15	10	25
Black or African American	204	99	303
Native Hawaiian or Other Pacific Islander	7	6	13
White	1428	722	2150
Mixed Origin	44	30	74
Unknown	19	6	25
Not Reported	18	5	23

End points

End points reporting groups

Reporting group title	Group 1: MenACYW conjugate vaccine

Reporting group description:

Group 1 was further randomized as Groups 1a and 1b based on the 4th dose timing, i.e. 12 to 15 months and 15 to 18 months respectively. Participants received MenACYW conjugate vaccine 0.5 milliliter (mL) as an intramuscular (IM) injection at 2, 4, 6, and 12 to 15 (Group 1a)/15-18 (Group 1b) months of age along with Pentacel® (diphtheria-tetanus-acellular pertussis [DTaP-IPV/Hib] vaccine) at 2, 4, 6 and 15 to 18 months of age; PREVNAR 13® (pneumococcal 13-valent conjugate vaccine [PCV13] at 2, 4, 6, and 12 to 15 months of age; RotaTeq® (pentavalent rotavirus vaccine [RV5]) at 2, 4, and 6 months of age; ENGERIX-B® (hepatitis B vaccine) at 2 and 6 months of age; M-M-R® II (measles, mumps, and rubella vaccine) and VARIVAX® (varicella vaccine) at 12 to 15 months of age. In addition to the above, Group 1b participants also received first dose of HAVRIX® (hepatitis A vaccine) at 15 to 18 months of age as a part of the study.

Reporting group title	Group 2: MENVEO

Reporting group description:

Group 2 was further randomized as Groups 2a and 2b based on the timing of blood collection, i.e. 12 and 15 months respectively. Participants received MENVEO conjugate vaccine 0.5 mL as an IM injection at 2, 4, 6, and 12 months of age along with Pentacel (DTaP-IPV/Hib vaccine) at 2, 4, 6 and 15 to 18 months of age; PREVNAR 13 (PCV13) at 2, 4, 6, and 12 months of age; RotaTeq (rotavirus vaccine) at 2, 4, and 6 months of age; ENGERIX-B (hepatitis B vaccine) at 2 and 6 months of age; M-M-R II (measles, mumps, and rubella vaccine) and VARIVAX (varicella vaccine) at 12 months of age. In addition, they also received first dose of HAVRIX (hepatitis A vaccine) at 15 to 18 months of age.

Subject analysis set title	Group 1a:MenACYW conjugate vaccine (post 12-month vaccination)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received MenACYW conjugate vaccine and routine vaccines at 2, 4, 6, and 12 to 15 months of age. The time of analyses as well as the collection of blood samples conducted in the 2nd year of life for this subgroup was 30 days after the 12-month vaccination.

Subject analysis set title	Group 1b:MenACYW conjugate vaccine(post 15-month vaccination)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received MenACYW conjugate vaccine at 2, 4, 6, and 15 to 18 months of age and routine vaccines at 2, 4, 6, 12 to 15 and 15 to 18 months of age. The time of analyses as well as the collection of blood samples conducted in the 2nd year of life for this subgroup was 30 days after the 15-month vaccination.

Subject analysis set title	Group 2a: MENVEO (post 12-month vaccination)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received MENVEO at 2, 4, 6, and 12 months of age and routine vaccines at 2, 4, 6, 12, and 15 to 18 months of age. The time of analyses as well as the collection of blood samples conducted in the 2nd year of life for this subgroup was 30 days after the 12-month vaccination.

Subject analysis set title	Group 2b: MENVEO (post 15-month vaccination)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received MENVEO at 2, 4, 6, and 12 months of age and routine vaccines at 2, 4, 6, 12, and 15 to 18 months of age. The time of analyses as well as the collection of blood samples conducted in the 2nd year of life for this subgroup was 30 days after the 15-month vaccination.

Primary: Groups 1a and 2a: Percentage of Participants With Vaccine Seroresponse Measured by hSBA at Day 30 Post 12-Month Vaccination

End point title	Groups 1a and 2a: Percentage of Participants With Vaccine Seroresponse Measured by hSBA at Day 30 Post 12-Month Vaccination

End point description:

Functional meningococcal antibody activity against serogroups A, C, Y, and W were measured in a serum bactericidal assay utilizing the hSBA. Vaccine seroresponse was defined as a post 4th dose (Day 30 after 12-month) hSBA titer >=1:16 for participants with pre 1st dose (Day 0 before 2-month) hSBA titer less than (<) 1:8, or at least a 4-fold increase in hSBA titer from pre-vaccination to post-vaccination for participants with pre-vaccination hSBA titer >=1:8. Analysis was performed on Per-Protocol Analysis Set 3 (PPAS3) (for 2nd year of life vaccination). PPAS3 included participants of Full Analysis set 3 (FAS3: a subset of all randomized participants who received >=1 dose of the study vaccine in the 2nd year of life [>=12 months of age] and had a valid post-vaccination serology result in the 2nd year of life) with no relevant protocol deviations. Only those participants with data collected are reported. Here, n=number of participants with data collected for each specific serogroup.

End point type	Primary

End point timeframe:

Day 30 post 12-month vaccination (Month 13)

End point values	Group 1a:MenACYW conjugate vaccine (post 12-month vaccination)	Group 2a: MENVEO (post 12-month vaccination)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	540	250		
Units: percentage of participants				
number (confidence interval 95%)				
Serogroup A (n=501, 223)	79.4 (75.6 to 82.9)	77.6 (71.5 to 82.9)		
Serogroup C (n=530, 238)	97.0 (95.1 to 98.3)	88.2 (83.4 to 92.0)		
Serogroup Y (n=523, 233)	96.4 (94.4 to 97.8)	92.3 (88.1 to 95.4)		
Serogroup W (n=540, 250)	97.6 (95.9 to 98.7)	96.4 (93.3 to 98.3)		

Statistical analyses

Statistical analysis title	Statistical analysis for Serogroup A

Statistical analysis description:

The overall non-inferiority was demonstrated if the lower limit of the 2-sided 95% confidence interval (CI) was >-10% for all 4 serogroups. 95% CI of the difference was calculated from the Wilson Score method without continuity correction.

Comparison groups	Group 1a:MenACYW conjugate vaccine (post 12-month vaccination) v Group 2a: MENVEO (post 12-month vaccination)
Number of subjects included in analysis	790
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in Percentage of Participants
Point estimate	1.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.38
upper limit	8.64

Statistical analysis title	Statistical analysis for Serogroup C

Statistical analysis description:

The overall non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI was >-10% for all 4 serogroups. 95% CI of the difference was calculated from the Wilson Score method without continuity correction.

Comparison groups	Group 1a:MenACYW conjugate vaccine (post 12-month vaccination) v Group 2a: MENVEO (post 12-month vaccination)
Number of subjects included in analysis	790
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in Percentage of Participants
Point estimate	8.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.8
upper limit	13.6

Statistical analysis title	Statistical analysis for Serogroup Y

Statistical analysis description:

The overall non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI was >-10% for all 4 serogroups. 95% CI of the difference was calculated from the Wilson Score method without continuity correction.

Comparison groups	Group 1a:MenACYW conjugate vaccine (post 12-month vaccination) v Group 2a: MENVEO (post 12-month vaccination)
Number of subjects included in analysis	790
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in Percentage of Participants
Point estimate	4.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	8.44

Statistical analysis title	Statistical analysis for Serogroup W

Statistical analysis description:

The overall non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI was >-10% for all 4 serogroups. 95% CI of the difference was calculated from the Wilson Score method without continuity correction.

Comparison groups	Group 1a:MenACYW conjugate vaccine (post 12-month vaccination) v Group 2a: MENVEO (post 12-month vaccination)

Number of subjects included in analysis	790
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in Percentage of Participants
Point estimate	1.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.18
upper limit	4.45

Primary: Groups 1 and 2: Percentage of Participants Who Achieved Antibody Titers >=1:8 by hSBA at Day 30 Post 6-Month Vaccination

End point title	Groups 1 and 2: Percentage of Participants Who Achieved Antibody Titers >=1:8 by hSBA at Day 30 Post 6-Month Vaccination

End point description:

Functional meningococcal antibody activity against serogroups A, C, Y, and W were measured in a serum bactericidal assay utilizing the hSBA. Analysis was performed on PPAS1 (for infant vaccination). PPAS1 included participants of FAS1 (subset of all randomized participants who received >=1 dose of the study vaccine in infancy [<12 months of age] and had a valid post-vaccination serology result in infancy) with no relevant protocol deviations during infancy. Only those participants with data collected are reported. Here, n=number of participants with data collected for each specific serogroup.

End point type	Primary

End point timeframe:

Day 30 post 6-month vaccination (Month 7)

End point values	Group 1: MenACYW conjugate vaccine	Group 2: MENVEO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	883	438		
Units: percentage of participants				
number (confidence interval 95%)				
Serogroup A (n=852, 409)	77.9 (75.0 to 80.7)	67.7 (63.0 to 72.2)		
Serogroup C (n=835, 421)	99.0 (98.1 to 99.6)	91.2 (88.1 to 93.7)		
Serogroup Y (n=861, 423)	98.3 (97.1 to 99.0)	91.7 (88.7 to 94.2)		
Serogroup W (n=883, 438)	98.6 (97.6 to 99.3)	92.9 (90.1 to 95.1)		

Statistical analyses

Statistical analysis title	Statistical analysis for Serogroup A

Statistical analysis description:

The overall non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI was >-10% for all 4 serogroups. 95% CI of the difference was calculated from the Wilson Score method without continuity correction.

Comparison groups	Group 1: MenACYW conjugate vaccine v Group 2: MENVEO
Number of subjects included in analysis	1321
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in Percentage of Participants
Point estimate	10.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.98
upper limit	15.59

Statistical analysis title	Statistical analysis for Serogroup C

Statistical analysis description:

The overall non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI was >-10% for all 4 serogroups. 95% CI of the difference was calculated from the Wilson Score method without continuity correction.

Comparison groups	Group 1: MenACYW conjugate vaccine v Group 2: MENVEO
Number of subjects included in analysis	1321
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in Percentage of Participants
Point estimate	7.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	5.31
upper limit	10.96

Statistical analysis title	Statistical analysis for Serogroup Y

Statistical analysis description:

The overall non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI was >-10% for all 4 serogroups. 95% CI of the difference was calculated from the Wilson Score method without continuity correction.

Comparison groups	Group 1: MenACYW conjugate vaccine v Group 2: MENVEO
Number of subjects included in analysis	1321
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in Percentage of Participants
Point estimate	6.53

Confidence interval	
level	95 %
sides	2-sided
lower limit	4.01
upper limit	9.62

Statistical analysis title	Statistical analysis for Serogroup W

Statistical analysis description:

The overall non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI was >-10% for all 4 serogroups. 95% CI of the difference was calculated from the Wilson Score method without continuity correction.

Comparison groups	Group 1: MenACYW conjugate vaccine v Group 2: MENVEO
Number of subjects included in analysis	1321
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in Percentage of Participants
Point estimate	5.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.44
upper limit	8.57

Secondary: Groups 1 and 2: Percentage of Participants who Achieved Anti-Hepatitis B Antibody Concentrations >=10 Milli-International Units per Milliliter (mIU/mL) at Day 30 Post 6-Month Vaccination

End point title	Groups 1 and 2: Percentage of Participants who Achieved Anti-Hepatitis B Antibody Concentrations >=10 Milli-International Units per Milliliter (mIU/mL) at Day 30 Post 6-Month Vaccination

End point description:

Anti-Hepatitis B surface antibodies (HBsAg) were measured by the commercially available VITROS ECi/ECiQ immunodiagnostic system using chemiluminescence detection technology. The percentage of participants with an anti-HBsAg antibody titer >=10 mIU/mL was assessed. Analysis was performed on PPAS1 (for infant vaccination) which included participants of FAS1 with no relevant protocol deviations during infancy. Only those participants with data collected are reported.

End point type	Secondary

End point timeframe:

Day 30 post 6-month vaccination (Month 7)

End point values	Group 1: MenACYW conjugate vaccine	Group 2: MENVEO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	765	348		
Units: percentage of participants				

number (confidence interval 95%)	98.6 (97.4 to 99.3)	98.0 (95.9 to 99.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Groups 1 and 2: Percentage of Participants who Achieved Anti-Polyribosyl-Ribitol (PRP) Antibody Concentrations >=0.15 and >=1.0 Microgram (mcg)/mL at Day 30 Post 6-Month Vaccination

End point title	Groups 1 and 2: Percentage of Participants who Achieved Anti-Polyribosyl-Ribitol (PRP) Antibody Concentrations >=0.15 and >=1.0 Microgram (mcg)/mL at Day 30 Post 6-Month Vaccination

End point description:

Anti-PRP concentrations were measured using a farr-type radioimmunoassay (RIA). The percentage of participants with an PRP antibody titer >=0.15 mcg/mL and >=1.0 mcg/mL were assessed. Analysis was performed on PPAS1 (for infant vaccination) which included participants of FAS1 with no relevant protocol deviations during infancy. Only those participants with data collected are reported.

End point type	Secondary

End point timeframe:

Day 30 post 6-month vaccination (Month 7)

End point values	Group 1: MenACYW conjugate vaccine	Group 2: MENVEO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	882	420		
Units: percentage of participants				
number (confidence interval 95%)				
>=0.15 mcg/mL	99.0 (98.1 to 99.5)	96.4 (94.2 to 98.0)		
>=1.0 mcg/mL	91.3 (89.2 to 93.0)	85.7 (82.0 to 88.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Groups 1 and 2: Percentage of Participants who Achieved Anti-Rotavirus Immunoglobulin A (IgA) Antibody Concentrations >=3-Fold Rise at Day 30 Post 6-Month Vaccination

End point title	Groups 1 and 2: Percentage of Participants who Achieved Anti-Rotavirus Immunoglobulin A (IgA) Antibody Concentrations >=3-Fold Rise at Day 30 Post 6-Month Vaccination

End point description:

Anti-rotavirus IgA antibodies in human serum were measured by enzyme-linked immunosorbent assay (ELISA). The percentage of participants who achieved anti-rotavirus IgA Ab concentrations >=3-fold rise were assessed. Analysis was performed on PPAS1 (for infant vaccination) which included participants of FAS1 with no relevant protocol deviations during infancy. Only those participants with data collected are reported.

End point type	Secondary

End point timeframe:

Day 30 post 6-month vaccination (Month 7)

End point values	Group 1: MenACYW conjugate vaccine	Group 2: MENVEO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	663	321		
Units: percentage of participants				
number (confidence interval 95%)	91.0 (88.5 to 93.0)	92.8 (89.4 to 95.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Groups 1 and 2: Geometric Mean Concentrations (GMCs) of Anti-Rotavirus IgA Antibodies at Day 30 Post 6-Month Vaccination

End point title	Groups 1 and 2: Geometric Mean Concentrations (GMCs) of Anti-Rotavirus IgA Antibodies at Day 30 Post 6-Month Vaccination

End point description:

GMCs of anti-rotavirus serum IgA antibodies were assessed using ELISA. Analysis was performed on PPAS1 (for infant vaccination) which included participants of FAS1 with no relevant protocol deviations during infancy. Only those participants with data collected are reported.

End point type	Secondary

End point timeframe:

Day 30 post 6-month vaccination (Month 7)

End point values	Group 1: MenACYW conjugate vaccine	Group 2: MENVEO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	857	403		
Units: U/mL				
geometric mean (confidence interval 95%)	272 (244 to 303)	308 (264 to 360)		

Statistical analyses

No statistical analyses for this end point

Secondary: Groups 1 and 2: Percentage of Participants who Achieved Anti-Poliovirus Antibody Titers >=1:8 at Day 30 Post 6-Month Vaccination

End point title	Groups 1 and 2: Percentage of Participants who Achieved Anti-Poliovirus Antibody Titers >=1:8 at Day 30 Post 6-Month Vaccination

End point description:

Anti-poliovirus types 1, 2, and 3 were measured by neutralization assay. The percentage of participants with anti-polio antibody titers >=1:8 were assessed. Analysis was performed on PPAS1 (for infant vaccination) which included participants of FAS1 with no relevant protocol deviations during infancy. Only those participants with data collected are reported. Here, n=number of participants with data collected for each specified category.

End point type	Secondary

End point timeframe:

Day 30 post 6-month vaccination (Month 7)

End point values	Group 1: MenACYW conjugate vaccine	Group 2: MENVEO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	854	415		
Units: percentage of participants				
number (confidence interval 95%)				
Anti-polio 1 (n=839, 412)	100 (99.6 to 100)	100 (99.1 to 100)		
Anti-polio 2 (n=838, 406)	100 (99.6 to 100)	100 (99.1 to 100)		
Anti-polio 3 (n=854, 415)	100 (99.6 to 100)	100 (99.1 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: Groups 1 and 2: GMCs of Anti-Pertussis Antibodies at Day 30 Post 6-Month Vaccination

End point title	Groups 1 and 2: GMCs of Anti-Pertussis Antibodies at Day 30 Post 6-Month Vaccination

End point description:

GMCs of anti-pertussis antibodies (pertussis toxoid [PT], filamentous hemagglutinin adhesin [FHA],

pertactin [PRN] and fimbriae types 2 and 3 [FIM]) were measured by electrochemiluminescent (ECL) assay. Analysis was performed on PPAS1 (for infant vaccination) which included participants of FAS1 with no relevant protocol deviations during infancy. Only those participants with data collected are reported.

End point type	Secondary

End point timeframe:

Day 30 post 6-month vaccination (Month 7)

End point values	Group 1: MenACYW conjugate vaccine	Group 2: MENVEO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	906	444		
Units: ELISA units/mL				
geometric mean (confidence interval 95%)				
Anti-PT	75.8 (72.2 to 79.6)	78.6 (72.8 to 84.9)		
Anti-FHA	95.7 (90.9 to 101)	98.6 (91.7 to 106)		
Anti-PRN	39.4 (36.8 to 42.3)	42.1 (37.9 to 46.6)		
Anti-FIM	309 (291 to 330)	311 (284 to 341)		

Statistical analyses

No statistical analyses for this end point

Secondary: Groups 1 and 2: GMCs of Anti-Pneumococcal Antibodies at Day 30 Post 6-Month Vaccination

End point title	Groups 1 and 2: GMCs of Anti-Pneumococcal Antibodies at Day 30 Post 6-Month Vaccination

End point description:

GMCs of anti-pneumococcal antibodies was assessed by pneumococcal capsular polysaccharide (PnPS) IgG ECL assay which is used to quantitate the amount of anti-streptococcus pneumoniae PS (serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F) antibodies in human serum. Analysis was performed on PPAS1 (for infant vaccination) which included participants of FAS1 with no relevant protocol deviations during infancy. Only those participants with data collected are reported. Here, n=number of participants with data collected for each serotype.

End point type	Secondary

End point timeframe:

Day 30 post 6-month vaccination (Month 7)

End point values	Group 1: MenACYW conjugate vaccine	Group 2: MENVEO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	874	420		
Units: mcg/mL				
geometric mean (confidence interval 95%)				
Serotype 1 (n=872, 420)	2.26 (2.13 to 2.40)	1.93 (1.77 to 2.12)		
Serotype 3 (n=869, 412)	0.607 (0.577 to 0.638)	0.544 (0.505 to 0.585)		
Serotype 4 (n=872, 420)	1.46 (1.40 to 1.53)	1.33 (1.24 to 1.42)		
Serotype 5 (n=873, 420)	1.54 (1.46 to 1.63)	1.26 (1.15 to 1.37)		
Serotype 6A (n=874, 420)	4.01 (3.82 to 4.22)	3.34 (3.09 to 3.62)		
Serotype 6B (n=874, 420)	2.47 (2.29 to 2.67)	1.97 (1.75 to 2.21)		
Serotype 7F (n=874, 419)	3.48 (3.32 to 3.64)	3.40 (3.18 to 3.63)		
Serotype 9V (n=873, 420)	1.88 (1.78 to 1.99)	1.61 (1.48 to 1.74)		
Serotype 14 (n=872, 420)	6.95 (6.53 to 7.41)	7.17 (6.58 to 7.81)		
Serotype 18C (n=874, 420)	1.95 (1.86 to 2.04)	1.82 (1.69 to 1.96)		
Serotype 19A (n=874, 420)	2.21 (2.10 to 2.32)	2.00 (1.86 to 2.14)		
Serotype 19F (n=874, 420)	3.36 (3.21 to 3.52)	2.98 (2.77 to 3.21)		
Serotype 23F (n=872, 420)	1.59 (1.49 to 1.69)	1.30 (1.18 to 1.44)		

Statistical analyses

No statistical analyses for this end point

Secondary: Groups 1a and 2a: Percentage of Participants who Achieved Vaccine Response for Varicella Antibodies at Day 30 Post 12-Month Vaccination

End point title	Groups 1a and 2a: Percentage of Participants who Achieved Vaccine Response for Varicella Antibodies at Day 30 Post 12-Month Vaccination

End point description:

Vaccine response against anti-varicella antibodies were measured by glycoprotein (gp) ELISA. Percentage of participants with anti-varicella antibody concentration >=5 antibody (Ab) gpELISA units/mL are reported. Analysis was performed on PPAS3 (for 2nd year of life vaccination) which included participants of FAS3 with no relevant protocol deviations. Only those participants with data collected are reported.

End point type	Secondary

End point timeframe:

Day 30 post 12-month vaccination (Month 13)

End point values	Group 1a:MenACYW conjugate vaccine (post 12-month vaccination)	Group 2a: MENVEO (post 12-month vaccination)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	662	301		
Units: percentage of participants				
number (confidence interval 95%)	96.4 (94.7 to 97.7)	94.7 (91.5 to 96.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Groups 1a and 2a: Percentage of Participants who Achieved Vaccine Response for Measles, Mumps and Rubella (MMR) Antibodies at Day 30 Post 12-Month Vaccination

End point title	Groups 1a and 2a: Percentage of Participants who Achieved Vaccine Response for Measles, Mumps and Rubella (MMR) Antibodies at Day 30 Post 12-Month Vaccination

End point description:

Vaccine response against anti-measles and anti-rubella antibodies were measured by bulk IgG enzyme immunoassay and anti-mumps antibodies were assessed by ELISA. Percentage of participants with anti-measles, anti-mumps, anti-rubella antibody concentration that met the respective mentioned criterion are reported: measles: >=255 mIU/mL; mumps: >=10 antibody units per milliliter and rubella: >=10 IU/mL. Analysis was performed on PPAS3 (for 2nd year of life vaccination) which included participants of FAS3 with no relevant protocol deviations. Only those participants with data collected are reported. Here, n=number of participants with data collected for each specified category.

End point type	Secondary

End point timeframe:

Day 30 post 12-month vaccination (Month 13)

End point values	Group 1a:MenACYW conjugate vaccine (post 12-month vaccination)	Group 2a: MENVEO (post 12-month vaccination)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	662	301		
Units: percentage of participants				
number (confidence interval 95%)				
Anti-measles (n=662, 301)	97.6 (96.1 to 98.6)	97.3 (94.8 to 98.8)		
Anti-mumps (n=660, 301)	95.5 (93.6 to 96.9)	97.7 (95.3 to 99.1)		

Anti-rubella (n=662, 301)	97.9 (96.5 to 98.8)	98.0 (95.7 to 99.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Groups 1a and 2a: GMCs of Anti-Pneumococcal Antibodies at Day 30 Post 12-Month Vaccination

End point title	Groups 1a and 2a: GMCs of Anti-Pneumococcal Antibodies at Day 30 Post 12-Month Vaccination

End point description:

GMCs of anti-pneumococcal antibodies was assessed by PnPS IgG ECL assay which is used to quantitate the amount of anti-streptococcus pneumoniae PS (serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F) antibodies in human serum. Analysis was performed on PPAS3 (for 2nd year of life vaccination) which included participants of FAS3 with no relevant protocol deviations. Only those participants with data collected are reported. Here, n=number of participants with data collected for each specific serogroup.

End point type	Secondary

End point timeframe:

Day 30 post 12-month vaccination (Month 13)

End point values	Group 1a:MenACYW conjugate vaccine (post 12-month vaccination)	Group 2a: MENVEO (post 12-month vaccination)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	653	300		
Units: mcg/mL				
geometric mean (confidence interval 95%)				
Serotype 1 (n=652, 299)	3.81 (3.56 to 4.08)	3.44 (3.12 to 3.81)		
Serotype 3 (n=651, 299)	0.771 (0.728 to 0.817)	0.751 (0.690 to 0.818)		
Serotype 4 (n=652, 299)	2.08 (1.95 to 2.22)	2.00 (1.83 to 2.18)		
Serotype 5 (n=652, 300)	2.70 (2.53 to 2.88)	2.46 (2.25 to 2.69)		
Serotype 6A (n=652, 300)	9.65 (9.09 to 10.2)	9.51 (8.72 to 10.4)		
Serotype 6B (n=649, 300)	7.41 (6.92 to 7.93)	6.37 (5.77 to 7.03)		
Serotype 7F (n=652, 298)	5.40 (5.08 to 5.73)	6.04 (5.56 to 6.55)		
Serotype 9V (n=652, 299)	3.53 (3.31 to 3.77)	3.62 (3.30 to 3.96)		
Serotype 14 (n=653, 300)	7.80 (7.26 to 8.38)	9.20 (8.37 to 10.1)		

Serotype 18C (n=652, 300)	2.60 (2.44 to 2.78)	2.92 (2.68 to 3.19)		
Serotype 19A (n=649, 300)	6.19 (5.82 to 6.59)	5.86 (5.32 to 6.45)		
Serotype 19F (n=652, 300)	6.49 (6.11 to 6.90)	6.01 (5.45 to 6.62)		
Serotype 23F (n=652, 300)	3.88 (3.60 to 4.17)	3.41 (3.09 to 3.78)		

Statistical analyses

No statistical analyses for this end point

Secondary: Groups 1b and 2b: Percentage of Participants who Achieved Vaccine Response for Anti-Pertussis Antibodies at Day 30 Post 15-Month Vaccination

End point title	Groups 1b and 2b: Percentage of Participants who Achieved Vaccine Response for Anti-Pertussis Antibodies at Day 30 Post 15-Month Vaccination

End point description:

Vaccine response was defined as: if the pre-booster (4th) vaccination concentration was <lower limit of quantification (LLOQ), then the post-booster (4th) vaccination concentration should be >= 4 times LLOQ. The LLOQ was equal to 2.00 EU/mL. Analysis was performed on PPAS3 (for 2nd year of life vaccination) which included participants of FAS3 with no relevant protocol deviations. Only those participants with data collected are reported.

End point type	Secondary

End point timeframe:

Day 30 post 15-month vaccination (Month 16)

End point values	Group 1b:MenACYW conjugate vaccine(post 15-month vaccination)	Group 2b: MENVEO (post 15-month vaccination)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	273	121		
Units: percentage of participants				
number (confidence interval 95%)				
Anti-PT	98.5 (96.3 to 99.6)	98.3 (94.2 to 99.8)		
Anti-FHA	96.7 (93.8 to 98.5)	96.7 (91.8 to 99.1)		
Anti-PRN	96.3 (93.4 to 98.2)	97.5 (92.9 to 99.5)		
Anti-FIM	98.2 (95.8 to 99.4)	97.5 (92.9 to 99.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Groups 1b and 2b: Percentage of Participants who Achieved Anti-Poliovirus Antibody Titers >=1:8 at Day 30 Post 15-Month Vaccination

End point title	Groups 1b and 2b: Percentage of Participants who Achieved Anti-Poliovirus Antibody Titers >=1:8 at Day 30 Post 15-Month Vaccination

End point description:

Anti-poliovirus types 1, 2, and 3 were measured by neutralization assay. The percentage of participants with anti-polio antibody titers >=1:8 are assessed. Analysis was performed on PPAS3 (for 2nd year of life vaccination) which included participants of FAS3 with no relevant protocol deviations. Only those participants with data collected are reported. Here, n=number of participants with data collected for each specified category.

End point type	Secondary

End point timeframe:

Day 30 post 15-month vaccination (Month 16)

End point values	Group 1b:MenACYW conjugate vaccine(post 15-month vaccination)	Group 2b: MENVEO (post 15-month vaccination)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	291	122		
Units: percentage of participants				
number (confidence interval 95%)				
Anti-polio 1 (n=286, 122)	100 (98.7 to 100)	100 (97.0 to 100)		
Anti-polio 2 (n=291, 122)	100 (98.7 to 100)	100 (97.0 to 100)		
Anti-polio 3 (n=289, 122)	100 (98.7 to 100)	100 (97.0 to 100)		

Statistical analyses

No statistical analyses for this end point

Secondary: Groups 1b and 2b: Percentage of Participants who Achieved Anti-PRP Antibody Concentrations >=1.0 mcg/mL at Day 30 Post 15-Month Vaccination

End point title	Groups 1b and 2b: Percentage of Participants who Achieved Anti-PRP Antibody Concentrations >=1.0 mcg/mL at Day 30 Post 15-Month Vaccination

End point description:

Anti-PRP concentrations were measured using a farr-type RIA. The percentage of participants with an PRP antibody titers >=1.0 mcg/mL were assessed. Analysis was performed on PPAS3 (for 2nd year of life vaccination) which included participants of FAS3 with no relevant protocol deviations. Only those participants with data collected are reported.

End point type	Secondary

End point timeframe:

Day 30 post 15-month vaccination (Month 16)

End point values	Group 1b:MenACYW conjugate vaccine(post 15-month vaccination)	Group 2b: MENVEO (post 15-month vaccination)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	297	125		
Units: percentage of participants				
number (confidence interval 95%)	98.3 (96.1 to 99.5)	98.4 (94.3 to 99.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Groups 1a and 2a: Geometric Mean Titers (GMTs) of Antibodies Against Meningococcal Serogroups A, C, Y, and W Measured by hSBA at Day 30 Post 6-Month Vaccination and Day 0 Before 12-Month Vaccination

End point title	Groups 1a and 2a: Geometric Mean Titers (GMTs) of Antibodies Against Meningococcal Serogroups A, C, Y, and W Measured by hSBA at Day 30 Post 6-Month Vaccination and Day 0 Before 12-Month Vaccination

End point description:

GMTs of antibody against meningococcal serogroups A, C, Y, and W were measured by hSBA. Analysis was performed on PPAS2 (for immunogenicity persistence evaluation). PPAS2 included participants of FAS2 (subset of all randomized participants who received >=1 dose of the study vaccine in infancy [at Visit 1 to 3, < 12 months of age] and had a valid pre-vaccination serology result at Visit 5 before the 12-month vaccinations for Subgroups 1a and 2a or at Visit 6 before the 15-month vaccinations for Subgroups 1b and 2b) with no relevant protocol deviations during infancy and for whom a pre-dose serology sample at Visit 5 for Subgroups 1a and 2a before the 12-month vaccinations or Visit 6 for Subgroups 1b and 2b before the 15-month vaccinations was not withdrawn. Only those participants with data collected are reported. Here, n=number of participants with data collected for each specified category; 3rd dose is 6-month vaccination and 4th dose is 12-month vaccination.

End point type	Secondary

End point timeframe:

Day 30 post 6-month vaccination (Month 7) and Day 0 before 12-month vaccination (Month 12)

End point values	Group 1a:MenACYW conjugate vaccine (post 12-month vaccination)	Group 2a: MENVEO (post 12-month vaccination)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	644	329		
Units: titer				
geometric mean (confidence interval 95%)				

Serogroup A: Day 30 post 3rd dose (n=547, 258)	24.9 (21.6 to 28.6)	16.3 (13.5 to 19.6)		
Serogroup A: Day 0 before 4th dose (n=627, 321)	9.33 (8.45 to 10.3)	6.43 (5.64 to 7.33)		
Serogroup C: Day 30 post 3rd dose (n=542, 268)	365 (325 to 411)	51.4 (42.9 to 61.5)		
Serogroup C: Day 0 before 4th dose (n=637, 324)	57.8 (51.5 to 64.8)	4.82 (4.22 to 5.50)		
Serogroup Y: Day 30 post 3rd dose (n=558, 270)	83.0 (75.0 to 91.8)	42.9 (36.7 to 50.0)		
Serogroup Y: Day 0 before 4th dose (n=633, 327)	42.9 (39.3 to 46.7)	10.4 (9.15 to 11.9)		
Serogroup W: Day 30 post 3rd dose (n=571, 277)	92.8 (84.8 to 102)	51.4 (43.9 to 60.0)		
Serogroup W: Day 0 before 4th dose (n=644, 329)	57.8 (52.7 to 63.3)	9.27 (8.15 to 10.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Groups 1a and 2a: Percentage of Participants Who Achieved Antibody Titers >=1:4 and >=1:8 Against Meningococcal Serogroups A, C, Y, and W at Day 30 Post 6-Month Vaccination and Day 0 Before 12-Month Vaccination

End point title	Groups 1a and 2a: Percentage of Participants Who Achieved Antibody Titers >=1:4 and >=1:8 Against Meningococcal Serogroups A, C, Y, and W at Day 30 Post 6-Month Vaccination and Day 0 Before 12-Month Vaccination

End point description:

Antibody titers of Meningococcal Serogroups A, C, Y, and W were measured by hSBA assay. Analysis was performed on PPAS2 (for immunogenicity persistence evaluation) which included participants of FAS2 with no relevant protocol deviations during infancy and for whom a pre-dose serology sample at Visit 5 for Subgroups 1a and 2a before the 12-month vaccinations or Visit 6 for Subgroups 1b and 2b before the 15-month vaccinations was not withdrawn. Only those participants with data collected are reported. Here, n=number of participants with data collected at each specified category, 3rd dose is 6-month vaccination, 4th dose is 12-month vaccination D0 is Day 0 and D30 is Day 30.

End point type	Secondary

End point timeframe:

Day 30 post 6-month vaccination (Month 7) and Day 0 before 12-month vaccination (Month 12)

End point values	Group 1a:MenACYW conjugate vaccine (post 12-month vaccination)	Group 2a: MENVEO (post 12-month vaccination)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	644	329		
Units: percentage of participants				
number (confidence interval 95%)				
Serogroup A: D30 post 3rd dose:>=1:4 (n=547,258)	87.0 (83.9 to 89.7)	84.9 (79.9 to 89.0)		
Serogroup A: D30 post 3rd dose:>=1:8 (n=547,258)	77.3 (73.6 to 80.8)	70.2 (64.2 to 75.7)		

Serogroup A:D0 before 4th dose:>=1:4(n=627,321)	82.5 (79.2 to 85.4)	66.4 (60.9 to 71.5)		
Serogroup A:D0 before 4th dose:>=1:8(n=627,321)	59.0 (55.0 to 62.9)	47.0 (41.5 to 52.7)		
Serogroup C: D30 post 3rd dose:>=1:4 (n=542,268)	99.3 (98.1 to 99.8)	93.7 (90.0 to 96.3)		
Serogroup C: D30 post 3rd dose:>=1:8 (n=542,268)	99.1 (97.9 to 99.7)	91.0 (87.0 to 94.2)		
Serogroup C:D0 before 4th dose:>=1:4(n=637,324)	95.4 (93.5 to 96.9)	49.1 (43.5 to 54.7)		
Serogroup C:D0 before 4th dose:>=1:8(n=637,324)	92.9 (90.7 to 94.8)	34.0 (28.8 to 39.4)		
Serogroup Y: D30 post 3rd dose:>=1:4 (n=558,270)	99.1 (97.9 to 99.7)	96.3 (93.3 to 98.2)		
Serogroup Y: D30 post 3rd dose:>=1:8 (n=558,270)	98.6 (97.2 to 99.4)	92.2 (88.4 to 95.1)		
Serogroup Y:D0 before 4th dose:>=1:4(n=633,327)	99.2 (98.2 to 99.7)	83.5 (79.0 to 87.3)		
Serogroup Y:D0 before 4th dose:>=1:8(n=633,327)	96.8 (95.2 to 98.1)	69.1 (63.8 to 74.1)		
Serogroup W: D30 post 3rd dose:>=1:4 (n=571,277)	99.8 (99.0 to 100)	97.5 (94.9 to 99.0)		
Serogroup W: D30 post 3rd dose:>=1:8 (n=571,277)	98.8 (97.5 to 99.5)	94.2 (90.8 to 96.7)		
Serogroup W:D0 before 4th dose:>=1:4(n=644,329)	98.9 (97.8 to 99.6)	82.7 (78.1 to 86.6)		
Serogroup W:D0 before 4th dose:>=1:8(n=644,329)	97.2 (95.6 to 98.3)	62.0 (56.5 to 67.3)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From start of study (Day 0) up to end of study (last point of contact [which included the 6-month safety follow up]), approximately 65 months

Adverse event reporting additional description:

Analysis was performed on SafAS which was defined as those participants who received at least 1 dose of the study vaccines and had any safety data available.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Group 2

Reporting group description:

Group 2 was further randomized as Groups 2a and 2b based on the timing of blood collection, i.e. 12 and 15 months respectively. Participants received MENVEO conjugate vaccine 0.5 mL as an IM injection at 2, 4, 6, and 12 months of age along with Pentacel (DTaP-IPV/Hib vaccine) at 2, 4, 6 and 15 to 18 months of age; PREVNAR 13 (PCV13) at 2, 4, 6, and 12 months of age; RotaTeq (rotavirus vaccine) at 2, 4, and 6 months of age; ENGERIX-B (hepatitis B vaccine) at 2 and 6 months of age; M-M-R II (measles, mumps, and rubella vaccine) and VARIVAX (varicella vaccine) at 12 months of age. In addition, they also received first dose of HAVRIX (hepatitis A vaccine) at 15 to 18 months of age.

Reporting group title	Group 1

Reporting group description:

Group 1 was further randomized as Groups 1a and 1b based on the 4th dose timing, i.e. 12 to 15 months and 15- 18 months respectively. Participants received MenACYW conjugate vaccine 0.5 mL as an IM injection at 2, 4, 6, and 12 to 15 (Group 1a)/15-18 (Group 1b) months of age along with Pentacel (diphtheria-tetanus-acellular pertussis [DTaP-IPV/Hib] vaccine) at 2, 4, 6 and 15 to 18 months of age; PREVNAR 13 (pneumococcal 13-valent conjugate vaccine [PCV13] at 2, 4, 6, and 12 to 15 months of age; RotaTeq (pentavalent rotavirus vaccine [RV5]) at 2, 4, and 6 months of age; ENGERIX-B (hepatitis B vaccine) at 2 and 6 months of age; M-M-R II (measles, mumps, and rubella vaccine) and VARIVAX (varicella vaccine) at 12 to 15 months of age. In addition to the above, Group 1b participants also received first dose of HAVRIX (hepatitis A vaccine) at 15 to 18 months of age as a part of the study.

Serious adverse events	Group 2	Group 1	
Total subjects affected by serious adverse events			
subjects affected / exposed	38 / 867 (4.38%)	99 / 1727 (5.73%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Glioma			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
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			

Craniocerebral Injury			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur Fracture			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post Vaccination Fever			
subjects affected / exposed	1 / 867 (0.12%)	0 / 1727 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head Injury			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper Limb Fracture			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural Haematoma			
subjects affected / exposed	0 / 867 (0.00%)	2 / 1727 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skull Fractured Base			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
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 / 867 (0.00%)	3 / 1727 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			

Congenital Absence Of Bile Ducts			
subjects affected / exposed	1 / 867 (0.12%)	0 / 1727 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Talipes			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urachal Abnormality			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyloric Stenosis			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac Arrest			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Epilepsy			
subjects affected / exposed	1 / 867 (0.12%)	0 / 1727 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid Haemorrhage			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure Like Phenomena			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Seizure			
subjects affected / exposed	1 / 867 (0.12%)	3 / 1727 (0.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile Convulsion			
subjects affected / exposed	3 / 867 (0.35%)	8 / 1727 (0.46%)	
occurrences causally related to treatment / all	0 / 4	1 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infantile Spasms			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Coagulopathy			
subjects affected / exposed	1 / 867 (0.12%)	0 / 1727 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sandifer's Syndrome			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal Reflux Disease			

subjects affected / exposed	0 / 867 (0.00%)	2 / 1727 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 867 (0.12%)	0 / 1727 (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 / 867 (0.00%)	1 / 1727 (0.06%)	
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			
Apnoea			
subjects affected / exposed	1 / 867 (0.12%)	0 / 1727 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute Respiratory Failure			
subjects affected / exposed	1 / 867 (0.12%)	2 / 1727 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory Distress			
subjects affected / exposed	3 / 867 (0.35%)	4 / 1727 (0.23%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspiration			

subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
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	0 / 867 (0.00%)	2 / 1727 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abscess Neck			
subjects affected / exposed	1 / 867 (0.12%)	0 / 1727 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenovirus Infection			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	1 / 867 (0.12%)	0 / 1727 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial Pyelonephritis			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bordetella Infection			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			

subjects affected / exposed	4 / 867 (0.46%)	15 / 1727 (0.87%)	
occurrences causally related to treatment / all	0 / 4	0 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
Covid-19			
subjects affected / exposed	1 / 867 (0.12%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 867 (0.12%)	0 / 1727 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Croup Infectious			
subjects affected / exposed	0 / 867 (0.00%)	2 / 1727 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eczema Coxsackium			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia Urinary Tract Infection			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Exanthema Subitum			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	3 / 867 (0.35%)	2 / 1727 (0.12%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis Norovirus			

subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis Viral			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal Viral Infection			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impetigo			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
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 / 867 (0.12%)	4 / 1727 (0.23%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis Media			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis Media Acute			
subjects affected / exposed	1 / 867 (0.12%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parainfluenzae Virus Infection			
subjects affected / exposed	0 / 867 (0.00%)	2 / 1727 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perirectal Abscess			

subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis Streptococcal			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral Infection			
subjects affected / exposed	1 / 867 (0.12%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary Tract Infection			
subjects affected / exposed	3 / 867 (0.35%)	2 / 1727 (0.12%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 867 (0.00%)	2 / 1727 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic Viral Infection			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic Infection			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal Scalded Skin Syndrome			

subjects affected / exposed	1 / 867 (0.12%)	0 / 1727 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin Bacterial Infection			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 867 (0.23%)	6 / 1727 (0.35%)	
occurrences causally related to treatment / all	0 / 2	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia Mycoplasmal			
subjects affected / exposed	1 / 867 (0.12%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia Viral			
subjects affected / exposed	0 / 867 (0.00%)	2 / 1727 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 867 (0.00%)	3 / 1727 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis Acute			
subjects affected / exposed	0 / 867 (0.00%)	2 / 1727 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory Syncytial Virus Bronchiolitis			
subjects affected / exposed	4 / 867 (0.46%)	9 / 1727 (0.52%)	
occurrences causally related to treatment / all	0 / 4	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory Syncytial Virus Infection			

subjects affected / exposed	6 / 867 (0.69%)	7 / 1727 (0.41%)	
occurrences causally related to treatment / all	0 / 6	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinovirus Infection			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Roseola			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 867 (0.00%)	1 / 1727 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Type 1 Diabetes Mellitus			
subjects affected / exposed	1 / 867 (0.12%)	0 / 1727 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ketoacidosis			
subjects affected / exposed	1 / 867 (0.12%)	0 / 1727 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	4 / 867 (0.46%)	3 / 1727 (0.17%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Group 2	Group 1	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	746 / 867 (86.04%)	1471 / 1727 (85.18%)	
Nervous system disorders			
Somnolence			
subjects affected / exposed	507 / 867 (58.48%)	975 / 1727 (56.46%)	
occurrences (all)	1273	2319	
General disorders and administration site conditions			
Injection Site Bruising			
subjects affected / exposed	88 / 867 (10.15%)	185 / 1727 (10.71%)	
occurrences (all)	158	380	
Injection Site Erythema			
subjects affected / exposed	409 / 867 (47.17%)	806 / 1727 (46.67%)	
occurrences (all)	2054	3898	
Injection Site Pain			
subjects affected / exposed	637 / 867 (73.47%)	1201 / 1727 (69.54%)	
occurrences (all)	5053	9341	
Injection Site Swelling			
subjects affected / exposed	323 / 867 (37.25%)	632 / 1727 (36.60%)	
occurrences (all)	1491	2651	
Pyrexia			
subjects affected / exposed	312 / 867 (35.99%)	580 / 1727 (33.58%)	
occurrences (all)	512	912	
Crying			
subjects affected / exposed	541 / 867 (62.40%)	1023 / 1727 (59.24%)	
occurrences (all)	1303	2366	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	196 / 867 (22.61%)	417 / 1727 (24.15%)	
occurrences (all)	276	607	
Teething			
subjects affected / exposed	62 / 867 (7.15%)	106 / 1727 (6.14%)	
occurrences (all)	73	124	
Psychiatric disorders			

Irritability			
subjects affected / exposed	598 / 867 (68.97%)	1154 / 1727 (66.82%)	
occurrences (all)	1694	3082	
Infections and infestations			
Otitis Media			
subjects affected / exposed	48 / 867 (5.54%)	79 / 1727 (4.57%)	
occurrences (all)	64	91	
Nasopharyngitis			
subjects affected / exposed	50 / 867 (5.77%)	96 / 1727 (5.56%)	
occurrences (all)	62	105	
Upper Respiratory Tract Infection			
subjects affected / exposed	130 / 867 (14.99%)	214 / 1727 (12.39%)	
occurrences (all)	162	264	
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	388 / 867 (44.75%)	704 / 1727 (40.76%)	
occurrences (all)	732	1246	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 March 2018	Updated cover page details and number of participants to be enrolled. Clarified how participants were randomized. Clarified that the 4th dose of Pentacel for Subgroup 1a was to be administered outside of the study by the study site personnel/Investigator. Modified existing primary objective; added an additional primary objective and added endpoint for rotavirus following Center for Biologics Evaluation and Research (CBER) protocol review received on 11 January 2018, also modified secondary objectives. Updated measles, mumps, and rubella endpoints with assay limits. Following CBER review/feedback; it was clarified that subgroup analyses was to be performed, presented in statistical analysis plan, an additional immunogenicity objective was added, planned sample size was updated, safety analysis after all 4 doses to observational objectives was included, power calculation was updated. Added and modified observational endpoints to correspond with observational objectives. Clarified exclusion criterion. Updated wording for statistical methods and hypothesis analysis to match the changes from objectives and endpoints. Updated the time window for Visits 02 and 03, and the age at Visit 03. in all tables. Deleted non-clinical safety section. Clarified visit procedure. Updated study calendar and randomization information. Added explanation of the role of the Sponsor's Safety Management Team. Updated text to reflect regulatory changes. Added new references for adverse events of special interest. Clarified safety and per protocol anlayses sets.
25 January 2019	Updated cover page details. Updated secondary and observational objectives and modified an inclusion criterion following CBER's comments. Modified an exclusion criterion. Product composition details modified. Mistake in value corrected. Added maternal immunization history as a study procedure. Wordings modified for clarity wherever necessary. Clarification added defining study vaccines. Modified definitions of analyses sets and updated package inserts.
02 June 2021	Updated cover page details and study period. During the study conduct, rather high attrition rate was noted especially during the Coronavirus Disease-2019 (COVID-19) pandemic year of 2020 which led the study team to increase the sample size for maintaining an acceptable overall power of primary and powered secondary hypotheses. Main factors of attrition were the visits outside of time windows, no blood draws performed at some visits and routine pediatric vaccines administration outside of the time window. No safety concerns were identified. Sample size was updated. The immunogenicity objectives initially listed as observational objectives were placed under secondary objectives. Added latest information on vaccine approval. Updated name of team member, the total number of participants to align with the updated sample size and study calendar. Minor changes to improve the clarity. A new section on a conditional sensitivity analysis was added to document the impact of COVID-19 pandemic situation on the study conduct.
26 January 2022	Cover page details updated. Updated the table on "History of Protocol Versions". Updated secondary endpoints and sensitivity analysis due to COVID-19 pandemic post feedback from CBER. Typo corrected in hypotheses section.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported