Clinical trial results:
Phase III, modified double-blind, randomized, parallel group, active-controlled, multi-center study to compare the immunogenicity of MenACYW conjugate vaccine with that of MENVEO®, describe the immunogenicity of MenACYW conjugate vaccine and Menactra®, and describe the safety of MenACYW conjugate vaccine, MENVEO®, and Menactra® when administered in a 1 + 1 schedule concomitantly with routine pediatric vaccines to healthy infants and toddlers in the United States

Summary

EudraCT number	2019-004460-22
Trial protocol	Outside EU/EEA
Global end of trial date	20 October 2023

Results information

Result version number	v1 (current)
This version publication date	28 April 2024
First version publication date	28 April 2024

Trial information

Trial identification

Sponsor protocol code	MET61

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03691610
WHO universal trial number (UTN)	U1111-1205-2836

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur Inc.
Sponsor organisation address	Discovery Drive, Swiftwater, Pennsylvania, 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	No

1901/2006 apply to this trial?	

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	08 January 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	20 October 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 vaccine seroresponse to meningococcal serogroups A, C, Y, and W following administration of 2 doses of MenACYW conjugate vaccine compared to 2 doses of MENVEO® when given concomitantly with routine pediatric vaccines to infants and toddlers 6 to 7 months of age (MoA) and 12 to 13 MoA.

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	04 October 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Puerto Rico: 21
Country: Number of subjects enrolled	United States: 929
Worldwide total number of subjects	950
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)	950
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 47 centers in the United States and Puerto Rico between 04 October 2018 and 23 October 2023.

Pre-assignment

Screening details:

A total of 950 participants were enrolled and randomized in 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	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Infants: Group 1

Arm description:

Participants received 2 doses of meningococcal polysaccharide (serogroups A, C, Y and W [MenACYW conjugate vaccine]) 0.5 milliliter (mL) intramuscular (IM) injection at 6 to 7 month of age (MoA) and 12 to 13 MoA, co-administered with pediatric vaccines recommended at this age.

Arm type	Experimental
Investigational medicinal product name	MenACYW conjugate vaccine
Investigational medicinal product code	
Other name	MenQuadfi®
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants were administered MenACYW conjugate vaccine 0.5 mL IM injection in the deltoid muscle of arm.

Arm title	Infants: Group 2

Arm description:

Participants received 2 doses of MENVEO® 0.5 mL IM injection at 6 to 7 MoA and 12 to 13 MoA, co-administered with pediatric vaccines recommended at this age.

Arm type	Active comparator
Investigational medicinal product name	MENVEO®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants were administered MENVEO® 0.5 mL IM injection in the deltoid muscle of arm.

Arm title	Toddlers: Group 3

Arm description:

Participants received 2 doses of meningococcal polysaccharide (serogroups A, C, Y and W [MenACYW conjugate vaccine]) 0.5 mL IM injection at 17 to 19 MoA and 20 to 23 MoA.

Arm type	Experimental

Investigational medicinal product name	MenACYW conjugate vaccine
Investigational medicinal product code	
Other name	MenQuadfi®
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants were administered MenACYW conjugate vaccine 0.5 mL IM injection in the deltoid muscle of arm.

Arm title	Toddlers: Group 4

Arm description:

Participants received 2 doses of Menactra® 0.5 mL IM injection at 17 to 19 MoA and 20 to 23 MoA.

Arm type	Active comparator
Investigational medicinal product name	Menactra®
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Participants were administered Menactra® 0.5 mL IM injection in the deltoid muscle of arm.

Number of subjects in period 1	Infants: Group 1	Infants: Group 2	Toddlers: Group 3
Started	380	370	96
Completed	298	290	83
Not completed	82	80	13
Adverse Event	-	1	-
Protocol Deviation	15	8	1
Withdrawal by Parent/Guardian	47	60	7
Lost to follow-up	20	11	5

Number of subjects in period 1	Toddlers: Group 4
Started	104
Completed	94
Not completed	10
Adverse Event	-
Protocol Deviation	2
Withdrawal by Parent/Guardian	6
Lost to follow-up	2

Baseline characteristics

Reporting groups	
Reporting group title	Infants: Group 1
Reporting group description:	
Participants received 2 doses of meningococcal polysaccharide (serogroups A, C, Y and W [MenACYW conjugate vaccine]) 0.5 milliliter (mL) intramuscular (IM) injection at 6 to 7 month of age (MoA) and 12 to 13 MoA, co-administered with pediatric vaccines recommended at this age.	
Reporting group title	Infants: Group 2
Reporting group description:	
Participants received 2 doses of MENVEO® 0.5 mL IM injection at 6 to 7 MoA and 12 to 13 MoA, co-administered with pediatric vaccines recommended at this age.	
Reporting group title	Toddlers: Group 3
Reporting group description:	
Participants received 2 doses of meningococcal polysaccharide (serogroups A, C, Y and W [MenACYW conjugate vaccine]) 0.5 mL IM injection at 17 to 19 MoA and 20 to 23 MoA.	
Reporting group title	Toddlers: Group 4
Reporting group description:	
Participants received 2 doses of Menactra® 0.5 mL IM injection at 17 to 19 MoA and 20 to 23 MoA.	

Reporting group values	Infants: Group 1	Infants: Group 2	Toddlers: Group 3
Number of subjects	380	370	96
Age Categorical			
Units: Subjects			
Age Continuous			
Units: months			
arithmetic mean	6.01	6.02	17.9
standard deviation	± 0.700	± 0.396	± 0.632
Gender Categorical			
Units: Subjects			
Female	180	172	48
Male	200	198	48
Race			
Units: Subjects			
American Indian or Alaska Native	0	1	0
Asian	6	6	2
Black or African American	70	68	11
Native Hawaiian or Other Pacific Islander	0	0	0
White	277	264	79
Mixed origin	14	20	4
Not Reported	10	4	0
Unknown	3	7	0

Reporting group values	Toddlers: Group 4	Total	
Number of subjects	104	950	
Age Categorical			
Units: Subjects			

Age Continuous Units: months			
arithmetic mean	17.9		
standard deviation	± 0.673	-	
Gender Categorical Units: Subjects			
Female	52	452	
Male	52	498	
Race Units: Subjects			
American Indian or Alaska Native	0	1	
Asian	1	15	
Black or African American	11	160	
Native Hawaiian or Other Pacific Islander	0	0	
White	87	707	
Mixed origin	5	43	
Not Reported	0	14	
Unknown	0	10	

End points

End points reporting groups

Reporting group title	Infants: Group 1
Reporting group description:	
Participants received 2 doses of meningococcal polysaccharide (serogroups A, C, Y and W [MenACYW conjugate vaccine]) 0.5 milliliter (mL) intramuscular (IM) injection at 6 to 7 month of age (MoA) and 12 to 13 MoA, co-administered with pediatric vaccines recommended at this age.	
Reporting group title	Infants: Group 2
Reporting group description:	
Participants received 2 doses of MENVEO® 0.5 mL IM injection at 6 to 7 MoA and 12 to 13 MoA, co-administered with pediatric vaccines recommended at this age.	
Reporting group title	Toddlers: Group 3
Reporting group description:	
Participants received 2 doses of meningococcal polysaccharide (serogroups A, C, Y and W [MenACYW conjugate vaccine]) 0.5 mL IM injection at 17 to 19 MoA and 20 to 23 MoA.	
Reporting group title	Toddlers: Group 4
Reporting group description:	
Participants received 2 doses of Menactra® 0.5 mL IM injection at 17 to 19 MoA and 20 to 23 MoA.	

Primary: Infants Groups 1 and 2: Percentage of Participants With Vaccine Seroresponse Measured by Serum Bactericidal Assay Using Human Complement (hSBA) at 30 Days Post Second Dose of MenACYW Conjugate Vaccine or MENVEO

End point title	Infants Groups 1 and 2: Percentage of Participants With Vaccine Seroresponse Measured by Serum Bactericidal Assay Using Human Complement (hSBA) at 30 Days Post Second Dose of MenACYW Conjugate Vaccine or MENVEO[1][2]

End point description:

Functional meningococcal antibody activity against serogroups A, C, Y, and W were measured in a serum bactericidal assay utilizing the hSBA. The hSBA vaccine seroresponse was defined as a post-vaccination titer >= 1:16 for participants with pre-vaccination hSBA titer < 1:8, or a post-vaccination titer >= 4-fold increase from baseline for participant with pre-vaccination hSBA titer >= 1:8. Per-protocol analysis set 2 (PPAS2) was a subset of the full analysis set 2 (FAS2). The FAS2 included all randomized participants who received at least 1 dose of the study vaccine in the second year of life (>= 12 MOA) and had a valid post vaccination serology result in the second year of life. Here, n= number of participants with available data for each specific serogroup.

End point type	Primary

End point timeframe:

Baseline (Day 0) and 30 days post second dose of MenACYW conjugate vaccine or MENVEO

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: As the endpoint is descriptive in nature, no statistical analysis is provided.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only infants randomized in Groups 1 and 2 were analyzed in the primary endpoint.

End point values	Infants: Group 1	Infants: Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	180	163		
Units: percentage of participants				
number (confidence interval 95%)				

Serogroup A (n=141, 123)	89.4 (83.1 to 93.9)	82.9 (75.1 to 89.1)		
Serogroup C (n=134, 126)	99.3 (95.9 to 100)	97.6 (93.2 to 99.5)		
Serogroup Y (n=140, 128)	98.6 (94.9 to 99.8)	97.7 (93.3 to 99.5)		
Serogroup W (n=143, 127)	99.3 (96.2 to 100)	92.9 (87.0 to 96.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Infants Groups 1 and 2: Percentage of Participants Who Achieved Antibody Titer (Seroprotection) >=1:8 by hSBA at 30 Days Post Second Dose of MenACYW Conjugate Vaccine or MENVEO

End point title	Infants Groups 1 and 2: Percentage of Participants Who Achieved Antibody Titer (Seroprotection) >=1:8 by hSBA at 30 Days Post Second Dose of MenACYW Conjugate Vaccine or MENVEO[3]

End point description:

Functional meningococcal antibody activity against serogroups A, C, Y, and W were measured in a serum bactericidal assay utilizing the hSBA. Seroprotection rate was defined as percentage of participants with hSBA titers >= 1:8. The PPAS2 was a subset of the FAS2. The FAS2 included all randomized participants who received at least 1 dose of the study vaccine in the second year of life (>= 12 MOA) and had a valid post vaccination serology result in the second year of life. Here, n= number of participants with available data for each specific serogroup.

End point type	Secondary

End point timeframe:

At 30 days post second dose of MenACYW conjugate vaccine or MENVEO

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only infants randomized in Groups 1 and 2 were analyzed in this secondary endpoint.

End point values	Infants: Group 1	Infants: Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	180	163		
Units: percentage of participants				
number (confidence interval 95%)				
Serogroup A (n=170, 158)	95.3 (90.9 to 97.9)	93.0 (87.9 to 96.5)		
Serogroup C (n=162, 160)	100 (97.7 to 100)	98.1 (94.6 to 99.6)		
Serogroup Y (n=170, 160)	100 (97.9 to 100)	97.5 (93.7 to 99.3)		
Serogroup W (n=171, 159)	100 (97.9 to 100)	95.6 (91.1 to 98.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Infants Groups 1 and 2: Percentage of Participants With hSBA Antibody Titer >= 1:4 and >= 1:8

End point title	Infants Groups 1 and 2: Percentage of Participants With hSBA Antibody Titer >= 1:4 and >= 1:8[4]

End point description:

Functional meningococcal antibody activity against serogroups A, C, Y, and W were measured in a serum bactericidal assay utilizing the hSBA. Participants with hSBA titers >= 1:4 and >= 1:8 were analyzed. Per-Protocol Analysis Set 1 (PPAS1) was a subset of full analysis set 1 (FAS1). FAS1 included all randomized participants who received at least 1 dose of study vaccine in infancy (< 12 MOA) and had a valid post vaccination serology result in infancy. PPAS2 analysis set. Per-Protocol Analysis Set 3 (PPAS3) was a subset of full analysis set 3 (FAS3). FAS3 included all randomized participants who received at least 1 dose of study vaccine in infancy (< 12 MOA) and had a valid pre-vaccination serology result at visit 3. Here, n= number of participants with available data for each specific serogroup.

End point type	Secondary

End point timeframe:

PPAS1: At 30 days post first dose; PPAS2: At Baseline (pre-dose on Day 0) and 30 days post second dose; and PPAS3: At 6 months post first dose of MenACYW conjugate vaccine or MENVEO

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only infants randomized in Groups 1 and 2 were analyzed in this secondary endpoint.

End point values	Infants: Group 1	Infants: Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	380	370		
Units: percentage of participants				
number (confidence interval 95%)				
PPAS1, Serogroup A: >=1:4 (n=130, 132)	64.6 (55.8 to 72.8)	55.3 (46.4 to 64.0)		
PPAS1, Serogroup A: >=1:8 (n=130, 132)	54.6 (45.7 to 63.4)	37.9 (29.6 to 46.7)		
PPAS1, Serogroup C: >=1:4 (n=127, 133)	96.9 (92.1 to 99.1)	93.2 (87.5 to 96.9)		
PPAS1, Serogroup C: >=1:8 (n=127, 133)	96.9 (92.1 to 99.1)	90.2 (83.9 to 94.7)		
PPAS1, Serogroup Y: >=1:4 (n=125, 128)	70.4 (61.6 to 78.2)	43.0 (34.3 to 52.0)		
PPAS1, Serogroup Y: >=1:8 (n=125, 128)	60.8 (51.7 to 69.4)	26.6 (19.1 to 35.1)		
PPAS1, Serogroup W: >=1:4 (n=134, 134)	49.3 (40.5 to 58.0)	37.3 (29.1 to 46.1)		
PPAS1, Serogroup W: >=1:8 (n=134, 134)	38.1 (29.8 to 46.8)	28.4 (20.9 to 36.8)		
PPAS2, Serogroup A, Day 0: >=1:4 (n=144, 127)	56.3 (47.7 to 64.5)	51.2 (42.2 to 60.1)		
PPAS2, Serogroup A, Day 0: >=1:8 (n=144, 127)	29.2 (21.9 to 37.3)	24.4 (17.2 to 32.8)		
PPAS2, Serogroup A, Day 30: >=1:4 (n=170, 158)	97.1 (93.3 to 99.0)	94.9 (90.3 to 97.8)		
PPAS2, Serogroup A, Day 30: >=1:8 (n=170, 158)	95.3 (90.9 to 97.9)	93.0 (87.9 to 96.5)		
PPAS2, Serogroup C, Day 0: >=1:4 (n=147, 129)	10.2 (5.8 to 16.3)	12.4 (7.3 to 19.4)		
PPAS2, Serogroup C, Day 0: >=1:8 (n=147, 129)	6.1 (2.8 to 11.3)	7.0 (3.2 to 12.8)		
PPAS2, Serogroup C, Day 30: >=1:4 (n=162, 160)	100 (97.7 to 100)	99.4 (96.6 to 100)		

PPAS2, Serogroup C, Day 30: >=1:8 (n=162, 160)	100 (97.7 to 100)	98.1 (94.6 to 99.6)		
PPAS2, Serogroup Y, Day 0: >=1:4 (n=149, 130)	15.4 (10.0 to 22.3)	12.3 (7.2 to 19.2)		
PPAS2, Serogroup Y, Day 0: >=1:8 (n=149, 130)	8.7 (4.7 to 14.5)	6.2 (2.7 to 11.8)		
PPAS2, Serogroup Y, Day 30: >=1:4 (n=170, 160)	100 (97.9 to 100)	98.1 (94.6 to 99.6)		
PPAS2, Serogroup Y, Day 30: >=1:8 (n=170, 160)	100 (97.9 to 100)	97.5 (93.7 to 99.3)		
PPAS2, Serogroup W, Day 0: >=1:4 (n=148, 130)	6.8 (3.3 to 12.1)	10.8 (6.0 to 17.4)		
PPAS2, Serogroup W, Day 0: >=1:8 (n=148, 130)	4.7 (1.9 to 9.5)	6.2 (2.7 to 11.8)		
PPAS2, Serogroup W, Day 30: >=1:4 (n=171, 159)	100 (97.9 to 100)	96.9 (92.8 to 99.0)		
PPAS2, Serogroup W, Day 30: >=1:8 (n=171, 159)	100 (97.9 to 100)	95.6 (91.1 to 98.2)		
PPAS3, Serogroup A: >=1:4 (n=103, 91)	87.4 (79.4 to 93.1)	85.7 (76.8 to 92.2)		
PPAS3, Serogroup A: >=1:8 (n=103, 91)	77.7 (68.4 to 85.3)	73.6 (63.3 to 82.3)		
PPAS3, Serogroup C: >=1:4 (n=104, 94)	99.0 (94.8 to 100)	77.7 (67.9 to 85.6)		
PPAS3, Serogroup C: >=1:8 (n=104, 94)	98.1 (93.2 to 99.8)	69.1 (58.8 to 78.3)		
PPAS3, Serogroup Y: >=1:4 (n=106, 93)	98.1 (93.4 to 99.8)	69.9 (59.5 to 79.0)		
PPAS3, Serogroup Y: >=1:8 (n=106, 93)	96.2 (90.6 to 99.0)	54.8 (44.2 to 65.2)		
PPAS3, Serogroup W: >=1:4 (n=106, 93)	98.1 (93.4 to 99.8)	61.3 (50.6 to 71.2)		
PPAS3, Serogroup W: >=1:8 (n=106, 93)	96.2 (90.6 to 99.0)	50.5 (40.0 to 61.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Infants Groups 1 and 2: Geometric Mean Titers Against Meningococcal Serogroups A, C, W, and Y

End point title	Infants Groups 1 and 2: Geometric Mean Titers Against Meningococcal Serogroups A, C, W, and Y[5]

End point description:

Functional meningococcal antibody activity against serogroups A, C, Y, and W were measured in a serum bactericidal assay utilizing the hSBA and the results were expressed as geometric mean titers. The PPAS1 was a subset of the FAS1. The FAS1 included all randomized participants who received at least 1 dose of the study vaccine in infancy (< 12 MOA) and had a valid post vaccination serology result in infancy. The PPAS2 was a subset of the FAS2. The FAS2 included all randomized participants who received at least 1 dose of the study vaccine in the second year of life (>= 12 MOA) and had a valid post vaccination serology result in the second year of life. The PPAS3 was a subset of the FAS3. The FAS3 included all randomized participants who received at least 1 dose of the study vaccine in infancy (< 12 MOA) and had a valid pre-vaccination serology result at visit 3. Here, n= number of participants with available data for each specific serogroup.

End point type	Secondary

End point timeframe:

PPAS1: At 30 days post first dose; PPAS2: At Baseline (pre-dose on Day 0) and 30 days post second dose; and PPAS3: At 6 months post first dose of MenACYW conjugate vaccine or MENVEO

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only infants randomized in Groups 1 and 2 were analyzed in this secondary endpoint.

End point values	Infants: Group 1	Infants: Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	380	370		
Units: titer				
geometric mean (confidence interval 95%)				
PPAS1: Serogroup A (n=130, 132)	8.26 (6.55 to 10.4)	5.45 (4.42 to 6.72)		
PPAS1: Serogroup C (n=127, 133)	167 (129 to 217)	41.3 (32.8 to 52.1)		
PPAS1: Serogroup Y (n=125, 128)	8.36 (6.61 to 10.6)	3.79 (3.20 to 4.49)		
PPAS1: Serogroup W (n=134, 134)	5.51 (4.39 to 6.92)	3.82 (3.22 to 4.52)		
PPAS2, Serogroup A: Day 0 (n=144, 127)	4.73 (3.92 to 5.72)	4.64 (3.74 to 5.74)		
PPAS2, Serogroup A: Day 30 (n=170, 158)	184 (143 to 237)	119 (90.6 to 157)		
PPAS2, Serogroup C: Day 0 (n=147, 129)	2.57 (2.21 to 2.99)	2.48 (2.20 to 2.79)		
PPAS2, Serogroup C: Day 30 (n=162, 160)	1473 (1236 to 1756)	319 (263 to 388)		
PPAS2, Serogroup Y: Day 0 (n=149, 130)	2.54 (2.27 to 2.83)	2.37 (2.16 to 2.60)		
PPAS2, Serogroup Y: Day 30 (n=170, 160)	423 (358 to 499)	133 (107 to 166)		
PPAS2, Serogroup W: Day 0 (n=148, 130)	2.23 (2.05 to 2.42)	2.31 (2.13 to 2.51)		
PPAS2, Serogroup W: Day 30 (n=171, 159)	442 (367 to 533)	106 (83.4 to 135)		
PPAS3: Serogroup A (n=103, 91)	20.1 (14.7 to 27.4)	14.9 (11.0 to 20.3)		
PPAS3: Serogroup C (n=104, 94)	150 (117 to 193)	12.7 (9.63 to 16.8)		
PPAS3: Serogroup Y (n=106, 93)	46.2 (36.3 to 58.6)	6.74 (5.43 to 8.36)		
PPAS3: Serogroup W (n=106, 93)	46.8 (36.1 to 60.5)	6.16 (4.87 to 7.80)		

Statistical analyses

No statistical analyses for this end point

Secondary: Infants Groups 1 and 2: Percentage of Participants With hSBA Antibody Titer >=1:4 to >= 1:128

End point title	Infants Groups 1 and 2: Percentage of Participants With hSBA Antibody Titer >=1:4 to >= 1:128[6]

End point description:

Functional meningococcal antibody activity against serogroups A, C, Y, and W were measured in a serum bactericidal assay utilizing the hSBA. Participants with hSBA titers >= 1:4 to >= 1:128 were analyzed. The PPAS1 was a subset of FAS1. The FAS1 included all randomized participants who received

at least 1 dose of the study vaccine in infancy (< 12 MOA) and had a valid post vaccination serology result in infancy. The PPAS2 was a subset of FAS2. The FAS2 included all randomized participants who received at least 1 dose of the study vaccine in the second year of life (>= 12 MOA) and had a valid post vaccination serology result in the second year of life. The PPAS3 was a subset of FAS3. The FAS3 included all randomized participants who received at least 1 dose of the study vaccine in infancy (< 12 MOA) and had a valid pre-vaccination serology result at visit 3. Here, n= number of participants with available data for each specific serogroup.

End point type	Secondary

End point timeframe:

PPAS1: At 30 days post first dose; PPAS2: At Baseline (pre-dose on Day 0) and 30 days post second dose; and PPAS3: At 6 months post first dose of MenACYW conjugate vaccine or MENVEO

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only infants randomized in Groups 1 and 2 were analyzed in this secondary endpoint.

End point values	Infants: Group 1	Infants: Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	380	370		
Units: percentage of participants				
number (not applicable)				
PPAS1, Serogroup A: >=1:4 (n= 130, 132)	64.6	55.3		
PPAS1, Serogroup A: >=1:128 (n= 130, 132)	3.1	3.0		
PPAS1, Serogroup C: >=1:4 (n= 127, 133)	96.9	93.2		
PPAS1, Serogroup C: >=1:128 (n= 127, 133)	67.7	32.3		
PPAS1, Serogroup Y: >=1:4 (n= 125, 128)	70.4	43.0		
PPAS1, Serogroup Y: >=1:128 (n= 125, 128)	5.6	0.8		
PPAS1, Serogroup W: >=1:4 (n= 134, 134)	49.3	37.3		
PPAS1, Serogroup W: >=1:128 (n= 134, 134)	4.5	0		
PPAS2, Serogroup A, Day 0: >=1:4 (n=144, 127)	56.3	51.2		
PPAS2, Serogroup A, Day 0: >=1:128 (n=144, 127)	4.9	3.1		
PPAS2, Serogroup A, Day 30: >=1:4 (n=170, 158)	97.1	94.9		
PPAS2, Serogroup A, Day 30: >=1:128 (n=170, 158)	68.8	62.7		
PPAS2, Serogroup C, Day 0: >=1:4 (n=147, 129)	10.2	12.4		
PPAS2, Serogroup C, Day 0: >=1:128 (n=147, 129)	2.0	0		
PPAS2, Serogroup C, Day 30: >=1:4 (n=162, 160)	100	99.4		
PPAS2, Serogroup C, Day 30: >=1:128 (n=162, 160)	98.1	88.1		
PPAS2, Serogroup Y, Day 0: >=1:4 (n=149, 130)	15.4	12.3		
PPAS2, Serogroup Y, Day 0: >=1:128 (n=149, 130)	0.7	0		
PPAS2, Serogroup Y, Day 30: >=1:4 (n=170, 160)	100	98.1		

PPAS2, Serogroup Y, Day 30: >=1:128 (n=170, 160)	90.0	58.8		
PPAS2, Serogroup W, Day 0: >=1:4 (n=148, 130)	6.8	10.8		
PPAS2, Serogroup W, Day 0: >=1:128 (n=148, 130)	0.7	0		
PPAS2, Serogroup W, Day 30: >=1:4 (n=171, 159)	100	96.9		
PPAS2, Serogroup W, Day 30: >=1:128 (n=171, 159)	90.6	56.0		
PPAS3, Serogroup A: >=1:4 (n=103, 91)	87.4	85.7		
PPAS3, Serogroup A: >=1:128 (n=103, 91)	18.4	12.1		
PPAS3, Serogroup C: >=1:4 (n=104, 94)	99.0	77.7		
PPAS3, Serogroup C: >=1:128 (n=104, 94)	69.2	6.4		
PPAS3, Serogroup Y: >=1:4 (n=106, 93)	98.1	69.9		
PPAS3, Serogroup Y: >=1:128 (n=106, 93)	27.4	1.1		
PPAS3, Serogroup W: >=1:4 (n=106, 93)	98.1	61.3		
PPAS3, Serogroup W: >=1:128 (n=106, 93)	33.0	3.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Infants Groups 1 and 2: Percentage of Participants With hSBA Antibody Titer >= 4-Fold Rise From Pre-Vaccination to Post-Vaccination

End point title	Infants Groups 1 and 2: Percentage of Participants With hSBA Antibody Titer >= 4-Fold Rise From Pre-Vaccination to Post-Vaccination[7]

End point description:

Functional meningococcal antibody activity against serogroups A, C, Y, and W were measured in a serum bactericidal assay utilizing the hSBA. Participants with hSBA titers >= 4-fold increase from baseline (pre-vaccination) were analyzed. The PPAS1 was a subset of the FAS1. The FAS1 included all randomized participants who received at least 1 dose of the study vaccine in infancy (< 12 MOA) and had a valid post vaccination serology result in infancy. The PPAS2 was a subset of the FAS2. The FAS2 included all randomized participants who received at least 1 dose of the study vaccine in the second year of life (>= 12 MOA) and had a valid post vaccination serology result in the second year of life. Here, n= number of participants with available data for each specific serogroup.

End point type	Secondary

End point timeframe:

PPAS1: At 30 days post first dose; and PPAS2: At 30 days post second dose of MenACYW conjugate vaccine or MENVEO

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Only infants randomized in Groups 1 and 2 were analyzed in this secondary endpoint.

End point values	Infants: Group 1	Infants: Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	380	370		
Units: percentage of participants				
number (confidence interval 95%)				
PPAS1: Serogroup A (n= 108, 111)	30.6 (22.1 to 40.2)	15.3 (9.2 to 23.4)		
PPAS1: Serogroup C (n= 104, 107)	92.3 (85.4 to 96.6)	81.3 (72.6 to 88.2)		
PPAS1: Serogroup Y (n= 102, 106)	30.4 (21.7 to 40.3)	7.5 (3.3 to 14.3)		
PPAS1: Serogroup W (n= 108, 112)	18.5 (11.7 to 27.1)	8.0 (3.7 to 14.7)		
PPAS2: Serogroup A (n= 141, 123)	89.4 (83.1 to 93.9)	82.9 (75.1 to 89.1)		
PPAS2: Serogroup C (n= 134, 126)	99.3 (95.9 to 100)	97.6 (93.2 to 99.5)		
PPAS2: Serogroup Y (n= 140, 128)	98.6 (94.9 to 99.8)	97.7 (93.3 to 99.5)		
PPAS2: Serogroup W (n= 143, 127)	99.3 (96.2 to 100)	92.9 (87.0 to 96.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Infants Groups 1 and 2: Percentage of Participants With Vaccine Seroresponse Measured by hSBA at 30 Days Post First Dose of MenACYW Conjugate Vaccine or MENVEO

End point title	Infants Groups 1 and 2: Percentage of Participants With Vaccine Seroresponse Measured by hSBA at 30 Days Post First Dose of MenACYW Conjugate Vaccine or MENVEO[8]

End point description:

Functional meningococcal antibody activity against serogroups A, C, Y, and W were measured in a serum bactericidal assay utilizing the hSBA. Participants with hSBA vaccine seroresponse which was defined as >= 4-fold increase from baseline (pre-vaccination) were analyzed. The PPAS1 was a subset of the FAS1. The FAS1 included all randomized participants who received at least 1 dose of the study vaccine in infancy (< 12 MOA) and had a valid post vaccination serology result in infancy. Here, n= number of participants with available data for each specific serogroup.

End point type	Secondary

End point timeframe:

At 30 days post first dose of MenACYW conjugate vaccine or MENVEO

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only infants randomized in Groups 1 and 2 were analyzed in this secondary endpoint.

End point values	Infants: Group 1	Infants: Group 2		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	135	138		
Units: percentage of participants				
number (confidence interval 95%)				

Serogroup A (n= 108, 111)	30.6 (22.1 to 40.2)	15.3 (9.2 to 23.4)		
Serogroup C (n= 104, 107)	92.3 (85.4 to 96.6)	81.3 (72.6 to 88.2)		
Serogroup Y (n= 102, 106)	30.4 (21.7 to 40.3)	7.5 (3.3 to 14.3)		
Serogroup W (n= 108, 112)	18.5 (11.7 to 27.1)	8.0 (3.7 to 14.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Toddlers Groups 3 and 4: Percentage of Participants With hSBA Antibody Titer >= 1:4 and >= 1:8

End point title	Toddlers Groups 3 and 4: Percentage of Participants With hSBA Antibody Titer >= 1:4 and >= 1:8[9]

End point description:

Functional meningococcal antibody activity against serogroups A, C, Y, and W were measured in a serum bactericidal assay utilizing the hSBA. Participants with hSBA titers >= 1:4 and >= 1:8 were analyzed. The PPAS2 was a subset of the FAS2. The FAS2 included all randomized participants who received at least 1 dose of the study vaccine in the second year of life (>= 12 MOA) and had a valid post vaccination serology result in the second year of life. Here, n= number of participants with available data for each specific serogroup.

End point type	Secondary

End point timeframe:

Baseline (Day 0) and 30 days post second dose of MenACYW conjugate vaccine or Menactra

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only toddlers randomized in Groups 3 and 4 were analyzed in this secondary endpoint.

End point values	Toddlers: Group 3	Toddlers: Group 4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	65		
Units: percentage of participants				
number (confidence interval 95%)				
Serogroup A, Day 0: >=1:4 (n=59, 59)	54.2 (40.8 to 67.3)	33.9 (22.1 to 47.4)		
Serogroup A, Day 0: >=1:8 (n=59, 59)	28.8 (17.8 to 42.1)	18.6 (9.7 to 30.9)		
Serogroup A, Day 30: >=1:4 (n=61, 64)	93.4 (84.1 to 98.2)	76.6 (64.3 to 86.2)		
Serogroup A, Day 30: >=1:8 (n=61, 64)	88.5 (77.8 to 95.3)	62.5 (49.5 to 74.3)		
Serogroup C, Day 0: >=1:4 (n=59, 59)	3.4 (0.4 to 11.7)	10.2 (3.8 to 20.8)		
Serogroup C, Day 0: >=1:8 (n=59, 59)	1.7 (0 to 9.1)	5.1 (1.1 to 14.1)		
Serogroup C, Day 30: >=1:4 (n=61, 65)	100 (94.1 to 100)	98.5 (91.7 to 100)		
Serogroup C, Day 30: >=1:8 (n=61, 65)	100 (94.1 to 100)	98.5 (91.7 to 100)		
Serogroup Y, Day 0: >=1:4 (n=59, 59)	11.9 (4.9 to 22.9)	10.2 (3.8 to 20.8)		

Serogroup Y, Day 0: >=1:8 (n=59, 59)	8.5 (2.8 to 18.7)	8.5 (2.8 to 18.7)		
Serogroup Y, Day 30: >=1:4 (n=61, 65)	100 (94.1 to 100)	93.8 (85.0 to 98.3)		
Serogroup Y, Day 30: >=1:8 (n=61, 65)	100 (94.1 to 100)	92.3 (83.0 to 97.5)		
Serogroup W, Day 0: >=1:4 (n=59, 59)	1.7 (0 to 9.1)	3.4 (0.4 to 11.7)		
Serogroup W, Day 0: >=1:8 (n=59, 59)	0 (0 to 6.1)	1.7 (0 to 9.1)		
Serogroup W, Day 30: >=1:4 (n=61, 65)	100 (94.1 to 100)	86.2 (75.3 to 93.5)		
Serogroup W, Day 30: >=1:8 (n=61, 65)	100 (94.1 to 100)	84.6 (73.5 to 92.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Toddlers Groups 3 and 4: Geometric Mean Titers Against Meningococcal Serogroups A, C, W, and Y

End point title	Toddlers Groups 3 and 4: Geometric Mean Titers Against Meningococcal Serogroups A, C, W, and Y[10]

End point description:

Functional meningococcal antibody activity against serogroups A, C, Y, and W were measured in a serum bactericidal assay utilizing the hSBA and the results were expressed as geometric mean titers. The PPAS2 was a subset of the FAS2. The FAS2 included all randomized participants who received at least 1 dose of the study vaccine in the second year of life (>= 12 MOA) and had a valid post vaccination serology result in the second year of life. Here, n= number of participants with available data for each specific serogroup.

End point type	Secondary

End point timeframe:

Baseline (Day 0) and 30 days post second dose of MenACYW conjugate vaccine or Menactra

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only toddlers randomized in Groups 3 and 4 were analyzed in this secondary endpoint.

End point values	Toddlers: Group 3	Toddlers: Group 4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	65		
Units: titer				
geometric mean (confidence interval 95%)				
Serogroup A: Day 0 (n=59, 59)	4.29 (3.36 to 5.49)	3.43 (2.61 to 4.51)		
Serogroup A: Day 30 (n=61, 64)	45.0 (29.8 to 68.0)	13.2 (8.72 to 19.9)		
Serogroup C: Day 0 (n=59, 59)	2.10 (1.95 to 2.26)	2.41 (2.01 to 2.90)		
Serogroup C: Day 30 (n=61, 65)	1727 (1300 to 2294)	59.4 (44.3 to 79.6)		
Serogroup Y: Day 0 (n=59, 59)	2.44 (2.07 to 2.88)	2.44 (2.05 to 2.91)		

Serogroup Y: Day 30 (n=61, 65)	284 (218 to 369)	45.5 (32.9 to 62.8)		
Serogroup W: Day 0 (n=59, 59)	2.02 (1.98 to 2.07)	2.12 (1.93 to 2.34)		
Serogroup W: Day 30 (n=61, 65)	202 (152 to 267)	25.0 (17.6 to 35.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Toddlers Groups 3 and 4: Percentage of Participants With hSBA Antibody Titer >= 1:4 to >= 1:128

End point title	Toddlers Groups 3 and 4: Percentage of Participants With hSBA Antibody Titer >= 1:4 to >= 1:128[11]

End point description:

Functional meningococcal antibody activity against serogroups A, C, Y, and W were measured in a serum bactericidal assay utilizing the hSBA. Participants with hSBA titers >= 1:4 to >= 1:128 were analyzed. The PPAS2 was a subset of the FAS2. The FAS2 included all randomized participants who received at least 1 dose of the study vaccine in the second year of life (>= 12 MOA) and had a valid post vaccination serology result in the second year of life. Here, n= number of participants with available data for each specific serogroup.

End point type	Secondary

End point timeframe:

Baseline (Day 0) and at 30 days post second dose of MenACYW conjugate vaccine or Menactra

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only toddlers randomized in Groups 3 and 4 were analyzed in this secondary endpoint.

End point values	Toddlers: Group 3	Toddlers: Group 4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	65		
Units: percentage of participants				
number (not applicable)				
Serogroup A, Day 0: >=1:4 (n=59, 59)	54.2	33.9		
Serogroup A, Day 0: >=1:128 (n=59, 59)	0	3.4		
Serogroup A, Day 30: >=1:4 (n=61, 64)	93.4	76.6		
Serogroup A, Day 30: >=1:128 (n=61, 64)	32.8	14.1		
Serogroup C, Day 0: >=1:4 (n=59, 59)	3.4	10.2		
Serogroup C, Day 0: >=1:128 (n=59, 59)	0	1.7		
Serogroup C, Day 30: >=1:4 (n=61, 65)	100	98.5		
Serogroup C, Day 30: >=1:128 (n=61, 65)	100	32.3		
Serogroup Y, Day 0: >=1:4 (n=59, 59)	11.9	10.2		
Serogroup Y, Day 0: >=1:128 (n=59, 59)	0	0		
Serogroup Y, Day 30: >=1:4 (n=61, 65)	100	93.8		

Serogroup Y, Day 30: >=1:128 (n=61, 65)	85.2	24.6		
Serogroup W, Day 0: >=1:4 (n=59, 59)	1.7	3.4		
Serogroup W, Day 0: >=1:128 (n=59, 59)	0	0		
Serogroup W, Day 30: >=1:4 (n=61, 65)	100	86.2		
Serogroup W, Day 30: >=1:128 (n=61, 65)	78.7	13.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Toddlers Groups 3 and 4: Percentage of Participants With hSBA Antibody Titer >= 4-Fold Rise From Pre-Vaccination to Post-Vaccination

End point title	Toddlers Groups 3 and 4: Percentage of Participants With hSBA Antibody Titer >= 4-Fold Rise From Pre-Vaccination to Post-Vaccination[12]

End point description:

Functional meningococcal antibody activity against serogroups A, C, Y, and W were measured in a serum bactericidal assay utilizing the hSBA. Participants with hSBA titers >= 4-fold increase from baseline (pre-vaccination) were analyzed. The PPAS2 was a subset of the FAS2. The FAS2 included all randomized participants who received at least 1 dose of the study vaccine in the second year of life (>= 12 MOA) and had a valid post vaccination serology result in the second year of life. Here, n= number of participants with available data for each specific serogroup.

End point type	Secondary

End point timeframe:

At 30 days post second dose of MenACYW conjugate vaccine or Menactra

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only toddlers randomized in Groups 3 and 4 were analyzed in this secondary endpoint.

End point values	Toddlers: Group 3	Toddlers: Group 4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	65		
Units: percentage of participants				
number (confidence interval 95%)				
Serogroup A (n= 59, 58)	72.9 (59.7 to 83.6)	46.6 (33.3 to 60.1)		
Serogroup C (n= 59, 59)	100 (93.9 to 100)	93.2 (83.5 to 98.1)		
Serogroup Y (n= 59, 59)	100 (93.9 to 100)	88.1 (77.1 to 95.1)		
Serogroup W (n= 59, 59)	100 (93.9 to 100)	76.3 (63.4 to 86.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Toddlers Groups 3 and 4: Percentage of Participants With Vaccine Seroresponse Measured by hSBA at 30 Days Post Second Dose of MenACYW conjugate vaccine or Menactra

End point title	Toddlers Groups 3 and 4: Percentage of Participants With Vaccine Seroresponse Measured by hSBA at 30 Days Post Second Dose of MenACYW conjugate vaccine or Menactra[13]

End point description:

Functional meningococcal antibody activity against serogroups A, C, Y, and W were measured in a serum bactericidal assay utilizing the hSBA. Participants with hSBA vaccine seroresponse which was defined as >= 4-fold increase from baseline (pre-vaccination) were analyzed. The PPAS2 was a subset of the FAS2. The FAS2 included all randomized participants who received at least 1 dose of the study vaccine in the second year of life (>= 12 MOA) and had a valid post vaccination serology result in the second year of life. Here, n= number of participants with available data for each specific serogroup.

End point type	Secondary

End point timeframe:

At 30 days post second dose of MenACYW conjugate vaccine or Menactra

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only toddlers randomized in Groups 3 and 4 were analyzed in this secondary endpoint.

End point values	Toddlers: Group 3	Toddlers: Group 4		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	65		
Units: percentage of participants				
number (confidence interval 95%)				
Serogroup A (n=59, 58)	72.9 (59.7 to 83.6)	46.6 (33.3 to 60.1)		
Serogroup C (n=59, 59)	100 (93.9 to 100)	93.2 (83.5 to 98.1)		
Serogroup Y (n=59, 59)	100 (93.9 to 100)	88.1 (77.1 to 95.1)		
Serogroup W (n=59, 59)	100 (93.9 to 100)	76.3 (63.4 to 86.4)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the first study vaccine administration (Day 0) up to 6 months after the last vaccination (Groups 1 and 2: up to 1846 days and Groups 3 and 4: up to 1109 days)

Adverse event reporting additional description:

Analysis was performed on the overall safety analysis set for any dose.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Infants: Group 1

Reporting group description:

Participants received 2 doses of meningococcal polysaccharide (serogroups A, C, Y and W [MenACYW conjugate vaccine]) 0.5 mL IM injection at 6 to 7 MoA and 12 to 13 MoA, co-administered with pediatric vaccines recommended at this age.

Reporting group title	Toddlers: Group 3

Reporting group description:

Participants received 2 doses of meningococcal polysaccharide (serogroups A, C, Y and W [MenACYW conjugate vaccine]) 0.5 mL IM injection at 17 to 19 MoA and 20 to 23 MoA.

Reporting group title	Toddlers: Group 4

Reporting group description:

Participants received 2 doses of Menactra® 0.5 mL IM injection at 17 to 19 MoA and 20 to 23 MoA.

Reporting group title	Infants: Group 2

Reporting group description:

Participants received 2 doses of MENVEO® 0.5 mL IM injection at 6 to 7 MoA and 12 to 13 MoA, co-administered with pediatric vaccines recommended at this age.

Serious adverse events	Infants: Group 1	Toddlers: Group 3	Toddlers: Group 4
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 370 (1.62%)	1 / 96 (1.04%)	4 / 103 (3.88%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute Myeloid Leukaemia			
subjects affected / exposed	0 / 370 (0.00%)	0 / 96 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Burns First Degree			

subjects affected / exposed	0 / 370 (0.00%)	0 / 96 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Accidental Exposure To Product			
subjects affected / exposed	0 / 370 (0.00%)	1 / 96 (1.04%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Febrile Convulsion			
subjects affected / exposed	1 / 370 (0.27%)	0 / 96 (0.00%)	2 / 103 (1.94%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Respiratory Depression			
subjects affected / exposed	0 / 370 (0.00%)	0 / 96 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess Limb			
subjects affected / exposed	1 / 370 (0.27%)	0 / 96 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis Bacterial			
subjects affected / exposed	1 / 370 (0.27%)	0 / 96 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis			
subjects affected / exposed	1 / 370 (0.27%)	0 / 96 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis Escherichia Coli			
subjects affected / exposed	0 / 370 (0.00%)	0 / 96 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Croup Infectious			
subjects affected / exposed	0 / 370 (0.00%)	0 / 96 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis Salmonella			
subjects affected / exposed	0 / 370 (0.00%)	0 / 96 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis Viral			
subjects affected / exposed	0 / 370 (0.00%)	0 / 96 (0.00%)	1 / 103 (0.97%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 370 (0.27%)	0 / 96 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia Parainfluenzae Viral			
subjects affected / exposed	0 / 370 (0.00%)	0 / 96 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory Syncytial Virus Bronchiolitis			
subjects affected / exposed	0 / 370 (0.00%)	0 / 96 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal Scalded Skin Syndrome			
subjects affected / exposed	1 / 370 (0.27%)	0 / 96 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral Infection			
subjects affected / exposed	0 / 370 (0.00%)	0 / 96 (0.00%)	0 / 103 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Infants: Group 2		
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 361 (3.32%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute Myeloid Leukaemia			
subjects affected / exposed	1 / 361 (0.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Burns First Degree			
subjects affected / exposed	1 / 361 (0.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Accidental Exposure To Product			
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Febrile Convulsion			
subjects affected / exposed	2 / 361 (0.55%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Respiratory Depression			
subjects affected / exposed	1 / 361 (0.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Abscess Limb			
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Arthritis Bacterial			

subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchiolitis			
subjects affected / exposed	2 / 361 (0.55%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis Escherichia Coli			
subjects affected / exposed	1 / 361 (0.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Croup Infectious			
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis Salmonella			
subjects affected / exposed	1 / 361 (0.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis Viral			
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia Parainfluenzae Viral			
subjects affected / exposed	1 / 361 (0.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory Syncytial Virus Bronchiolitis			

subjects affected / exposed	2 / 361 (0.55%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Staphylococcal Scalded Skin Syndrome			
subjects affected / exposed	0 / 361 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Viral Infection			
subjects affected / exposed	1 / 361 (0.28%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Infants: Group 1	Toddlers: Group 3	Toddlers: Group 4
Total subjects affected by non-serious adverse events			
subjects affected / exposed	288 / 370 (77.84%)	68 / 96 (70.83%)	74 / 103 (71.84%)
Nervous system disorders			
Somnolence			
subjects affected / exposed	160 / 370 (43.24%)	28 / 96 (29.17%)	30 / 103 (29.13%)
occurrences (all)	208	41	36
General disorders and administration site conditions			
Crying			
subjects affected / exposed	160 / 370 (43.24%)	35 / 96 (36.46%)	34 / 103 (33.01%)
occurrences (all)	200	45	45
Injection Site Bruising			
subjects affected / exposed	19 / 370 (5.14%)	3 / 96 (3.13%)	3 / 103 (2.91%)
occurrences (all)	35	3	4
Injection Site Erythema			
subjects affected / exposed	151 / 370 (40.81%)	29 / 96 (30.21%)	26 / 103 (25.24%)
occurrences (all)	479	41	37
Injection Site Pain			
subjects affected / exposed	202 / 370 (54.59%)	43 / 96 (44.79%)	41 / 103 (39.81%)
occurrences (all)	782	65	60

Injection Site Swelling			
subjects affected / exposed	125 / 370 (33.78%)	23 / 96 (23.96%)	14 / 103 (13.59%)
occurrences (all)	361	34	19
Pyrexia			
subjects affected / exposed	68 / 370 (18.38%)	18 / 96 (18.75%)	20 / 103 (19.42%)
occurrences (all)	83	28	23
Gastrointestinal disorders			
Teething			
subjects affected / exposed	29 / 370 (7.84%)	1 / 96 (1.04%)	3 / 103 (2.91%)
occurrences (all)	44	1	3
Vomiting			
subjects affected / exposed	44 / 370 (11.89%)	8 / 96 (8.33%)	10 / 103 (9.71%)
occurrences (all)	50	9	10
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	11 / 370 (2.97%)	6 / 96 (6.25%)	1 / 103 (0.97%)
occurrences (all)	11	7	1
Psychiatric disorders			
Irritability			
subjects affected / exposed	202 / 370 (54.59%)	44 / 96 (45.83%)	52 / 103 (50.49%)
occurrences (all)	289	65	74
Infections and infestations			
Influenza			
subjects affected / exposed	1 / 370 (0.27%)	5 / 96 (5.21%)	1 / 103 (0.97%)
occurrences (all)	1	5	1
Nasopharyngitis			
subjects affected / exposed	20 / 370 (5.41%)	1 / 96 (1.04%)	0 / 103 (0.00%)
occurrences (all)	22	1	0
Otitis Media			
subjects affected / exposed	15 / 370 (4.05%)	5 / 96 (5.21%)	5 / 103 (4.85%)
occurrences (all)	17	5	5
Upper Respiratory Tract Infection			
subjects affected / exposed	41 / 370 (11.08%)	3 / 96 (3.13%)	4 / 103 (3.88%)
occurrences (all)	45	4	4
Metabolism and nutrition disorders			

Decreased Appetite			
subjects affected / exposed	83 / 370 (22.43%)	28 / 96 (29.17%)	34 / 103 (33.01%)
occurrences (all)	104	36	47

Non-serious adverse events	Infants: Group 2		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	257 / 361 (71.19%)		
Nervous system disorders			
Somnolence			
subjects affected / exposed	157 / 361 (43.49%)		
occurrences (all)	218		
General disorders and administration site conditions			
Crying			
subjects affected / exposed	138 / 361 (38.23%)		
occurrences (all)	179		
Injection Site Bruising			
subjects affected / exposed	13 / 361 (3.60%)		
occurrences (all)	17		
Injection Site Erythema			
subjects affected / exposed	138 / 361 (38.23%)		
occurrences (all)	460		
Injection Site Pain			
subjects affected / exposed	180 / 361 (49.86%)		
occurrences (all)	691		
Injection Site Swelling			
subjects affected / exposed	105 / 361 (29.09%)		
occurrences (all)	331		
Pyrexia			
subjects affected / exposed	71 / 361 (19.67%)		
occurrences (all)	81		
Gastrointestinal disorders			
Teething			
subjects affected / exposed	25 / 361 (6.93%)		
occurrences (all)	42		
Vomiting			
subjects affected / exposed	39 / 361 (10.80%)		
occurrences (all)	41		

Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	 6 / 361 (1.66%) 8		
Psychiatric disorders Irritability subjects affected / exposed occurrences (all)	 186 / 361 (51.52%) 264		
Infections and infestations Influenza subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Otitis Media subjects affected / exposed occurrences (all) Upper Respiratory Tract Infection subjects affected / exposed occurrences (all)	 0 / 361 (0.00%) 0 11 / 361 (3.05%) 16 14 / 361 (3.88%) 17 40 / 361 (11.08%) 44		
Metabolism and nutrition disorders Decreased Appetite subjects affected / exposed occurrences (all)	 83 / 361 (22.99%) 102		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
04 March 2021	WIP
12 May 2022	WIP

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported