Clinical trial results:
Immunogenicity and Safety of an Investigational Quadrivalent Meningococcal Conjugate Vaccine Administered in Healthy Children 2 to 9 Years of Age

Summary

EudraCT number	2018-001471-20
Trial protocol	Outside EU/EEA
Global end of trial date	10 October 2017

Results information

Result version number	v1 (current)
This version publication date	29 December 2018
First version publication date	29 December 2018

Trial information

Trial identification

Sponsor protocol code	MET35

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03077438
WHO universal trial number (UTN)	U1111-1161-2625

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur Inc.
Sponsor organisation address	1 Discovery Drive, Swiftwater, United States, 18370
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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	12 April 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 October 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the non-inferiority of the vaccine seroresponse to meningococcal serogroups A, C, Y, and W following the administration of a single dose of Meningococcal Polysaccharide (Serogroups A, C, Y and W) Tetanus Toxoid (MenACYW) compared to that observed following the administration of a single dose of MENVEO® in children aged 2 to 9 years.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 February 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 1000
Worldwide total number of subjects	1000
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)	0
Children (2-11 years)	1000
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:

Study subjects were enrolled in 36 centers in the Unites States (US) and Puerto Rico from 17 February 2017 to 30 March 2017.

Pre-assignment

Screening details:

A total of 1000 subjects who met all of the inclusion criteria and none of the exclusion criteria 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	Group 1: MenACYW Conjugate Vaccine

Arm description:

Healthy, meningococcal-vaccine naïve subjects aged 2 to 9 years received a single dose of MenACYW conjugate vaccine.

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

Dosage and administration details:

0.5 mL, intramuscular, single dose on Day 0.

Arm title	Group 2: MENVEO® Vaccine

Arm description:

Healthy, meningococcal-vaccine naïve subjects aged 2 to 9 years received a single dose of MENVEO® vaccine.

Arm type	Active comparator
Investigational medicinal product name	MENVEO®: Meningococcal (Groups A, C, Y and W-135) Oligosaccharide Diphtheria CRM197 Conjugate Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, single dose on Day 0.

Number of subjects in period 1	Group 1: MenACYW Conjugate Vaccine	Group 2: MENVEO® Vaccine
Started	499	501
Safety analysis set	498	494
Completed	487	487
Not completed	12	14
Consent withdrawn by subject	3	6
Lost to follow-up	6	3
Protocol deviation	3	5

Baseline characteristics

Reporting groups	
Reporting group title	Group 1: MenACYW Conjugate Vaccine
Reporting group description:	
Healthy, meningococcal-vaccine naïve subjects aged 2 to 9 years received a single dose of MenACYW conjugate vaccine.	
Reporting group title	Group 2: MENVEO® Vaccine
Reporting group description:	
Healthy, meningococcal-vaccine naïve subjects aged 2 to 9 years received a single dose of MENVEO® vaccine.	

Reporting group values	Group 1: MenACYW Conjugate Vaccine	Group 2: MENVEO® Vaccine	Total
Number of subjects	499	501	1000
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	499	501	1000
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	6.0	6.0	
standard deviation	± 2.33	± 2.36	-
Gender categorical			
Units: Subjects			
Female	245	236	481
Male	254	265	519
Region of Enrollment			
Units: Subjects			
United States	499	501	1000

End points

End points reporting groups

Reporting group title	Group 1: MenACYW Conjugate Vaccine
Reporting group description:	
Healthy, meningococcal-vaccine naïve subjects aged 2 to 9 years received a single dose of MenACYW conjugate vaccine.	
Reporting group title	Group 2: MENVEO® Vaccine
Reporting group description:	
Healthy, meningococcal-vaccine naïve subjects aged 2 to 9 years received a single dose of MENVEO® vaccine.	

Primary: Percentages of Subjects Achieving Serum Bactericidal Assay Using Human Complement (hSBA) Vaccine Seroresponse for Meningococcal Serogroups A, C, Y, and W Following Vaccination With Either MenACYW Conjugate Vaccine or MENVEO® Vaccine

End point title	Percentages of Subjects Achieving Serum Bactericidal Assay Using Human Complement (hSBA) Vaccine Seroresponse for Meningococcal Serogroups A, C, Y, and W Following Vaccination With Either MenACYW Conjugate Vaccine or MENVEO® Vaccine
End point description:	
Antibody titers against meningococcal serogroups A, C, Y, and W measured by hSBA. The hSBA vaccine seroresponse for serogroups A, C, Y, and W was defined as post-vaccination hSBA titers >=1:16 for subjects with pre-vaccination hSBA titers <1:8 or at least a 4-fold increase in hSBA titers from pre- to post-vaccination for subjects with pre-vaccination hSBA titers >=1:8. Analysis was performed on Per-Protocol Analysis Set (PPAS) defined for accessing the ACYW immune response data for all subjects who received at least one dose of study vaccine and had a valid post-vaccination serology result. The subjects who presented pre-defined protocol deviations were excluded from per-protocol analysis set. Here 'n' signifies number of subjects with available data for specified category.	
End point type	Primary
End point timeframe:	
Day 30 (post-vaccination)	

End point values	Group 1: MenACYW Conjugate Vaccine	Group 2: MENVEO® Vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	458	460		
Units: percentage of subjects				
number (confidence interval 95%)				
Serogroup A (n=455,458)	55.4 (50.7 to 60.0)	47.8 (43.2 to 52.5)		
Serogroup C (n=458,458)	95.2 (92.8 to 97.0)	47.8 (43.2 to 52.5)		
Serogroup Y (n=458,459)	91.5 (88.5 to 93.9)	79.3 (75.3 to 82.9)		
Serogroup W (n=458,459)	78.8 (74.8 to 82.5)	64.1 (59.5 to 68.4)		

Statistical analyses

Statistical analysis title	Serogroup A
Statistical analysis description:	
Actual number of subjects analyzed = 913	
Comparison groups	Group 1: MenACYW Conjugate Vaccine v Group 2: MENVEO® Vaccine
Number of subjects included in analysis	918
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Percentage Difference
Point estimate	7.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.1
upper limit	14

Notes:

[1] - 95% confidence interval (CI) of the difference was calculated from the Wilson Score Method without continuity correction. Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI of the difference between the 2 percentages was >-10%.

Statistical analysis title	Serogroup C
Statistical analysis description:	
Actual number of subjects analyzed = 916	
Comparison groups	Group 1: MenACYW Conjugate Vaccine v Group 2: MENVEO® Vaccine
Number of subjects included in analysis	918
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Percentage Difference
Point estimate	47.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	42.2
upper limit	52.2

Notes:

[2] - 95% CI of the difference was calculated from the Wilson Score Method without continuity correction. Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI of the difference between the 2 percentages was >-10%.

Statistical analysis title	Serogroup Y
Statistical analysis description:	
Actual number of subjects analyzed = 917	
Comparison groups	Group 1: MenACYW Conjugate Vaccine v Group 2: MENVEO® Vaccine

Number of subjects included in analysis	918
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Percentage Difference
Point estimate	12.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.7
upper limit	16.7

Notes:

[3] - 95% CI of the difference was calculated from the Wilson Score Method without continuity correction. Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI of the difference between the 2 percentages was >-10%.

Statistical analysis title	Serogroup W

Statistical analysis description:

Actual number of subjects analyzed = 917

Comparison groups	Group 1: MenACYW Conjugate Vaccine v Group 2: MENVEO® Vaccine
Number of subjects included in analysis	918
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Parameter estimate	Percentage Difference
Point estimate	14.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.9
upper limit	20.5

Notes:

[4] - 95% CI of the difference was calculated from the Wilson Score Method without continuity correction. Non-inferiority was demonstrated if the lower limit of the 2-sided 95% CI of the difference between the 2 percentages was >-10%.

Secondary: Geometric Mean Titers (GMTs) of Meningococcal Serogroups A, C, Y, and W Antibodies Following Vaccination With Either MenACYW Conjugate Vaccine or MENVEO® Vaccine in Children 2 to 9 Years of Age

End point title	Geometric Mean Titers (GMTs) of Meningococcal Serogroups A, C, Y, and W Antibodies Following Vaccination With Either MenACYW Conjugate Vaccine or MENVEO® Vaccine in Children 2 to 9 Years of Age

End point description:

Antibody titers against meningococcal serogroups A, C, Y, and W measured by hSBA. Analysis was performed on PPAS. Here 'n' signifies number of subjects with available data for specified category.

End point type	Secondary

End point timeframe:

Day 30 (post-vaccination)

End point values	Group 1: MenACYW Conjugate Vaccine	Group 2: MENVEO® Vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	458	460		
Units: titers				
geometric mean (confidence interval 95%)				
Serogroup A (n=456,458)	24.8 (21.9 to 27.9)	22.6 (19.7 to 26.0)		
Serogroup C (n=458,459)	238 (209 to 270)	17.0 (14.3 to 20.2)		
Serogroup Y (n=458,459)	68.8 (61.3 to 77.3)	43.5 (37.7 to 50.4)		
Serogroup W (n=458,459)	37.5 (33.7 to 41.8)	26.2 (23.0 to 29.9)		

Statistical analyses

Statistical analysis title	Serogroup A
Statistical analysis description: Actual number of subjects analyzed = 914	
Comparison groups	Group 2: MENVEO® Vaccine v Group 1: MenACYW Conjugate Vaccine
Number of subjects included in analysis	918
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT Ratio
Point estimate	1.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.32

Statistical analysis title	Serogroup C
Statistical analysis description: Actual number of subjects analyzed = 917	
Comparison groups	Group 1: MenACYW Conjugate Vaccine v Group 2: MENVEO® Vaccine
Number of subjects included in analysis	918
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT Ratio
Point estimate	14

Confidence interval	
level	95 %
sides	2-sided
lower limit	11.3
upper limit	17.3

Statistical analysis title	Serogroup Y
Statistical analysis description:	
Actual number of subjects analyzed = 917	
Comparison groups	Group 1: MenACYW Conjugate Vaccine v Group 2: MENVEO® Vaccine
Number of subjects included in analysis	918
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT Ratio
Point estimate	1.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.31
upper limit	1.9

Statistical analysis title	Serogroup W
Statistical analysis description:	
Actual number of subjects analyzed = 917	
Comparison groups	Group 1: MenACYW Conjugate Vaccine v Group 2: MENVEO® Vaccine
Number of subjects included in analysis	918
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT Ratio
Point estimate	1.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.21
upper limit	1.69

Secondary: GMTs of Meningococcal Serogroups A, C, Y, and W Antibodies Following Vaccination With Either MenACYW Conjugate Vaccine or MENVEO® Vaccine in Children 2 to 5 Years of Age

End point title	GMTs of Meningococcal Serogroups A, C, Y, and W Antibodies Following Vaccination With Either MenACYW Conjugate Vaccine or MENVEO® Vaccine in Children 2 to 5 Years of Age

End point description:

Antibody titers against meningococcal serogroups A, C, Y, and W measured by hSBA. Analysis was performed on PPAS. Here 'Number of subjects analysed' signifies number of subjects in the PPAS aged 2-5 years, and 'n' signifies number of subjects with available data for specified category.

End point type	Secondary

End point timeframe:

Day 30 (post-vaccination)

End point values	Group 1: MenACYW Conjugate Vaccine	Group 2: MENVEO® Vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	229	223		
Units: titers				
geometric mean (confidence interval 95%)				
Serogroup A (n=228,221)	21.6 (18.2 to 25.5)	18.9 (15.5 to 23.0)		
Serogroup C (n=229,223)	208 (175 to 246)	11.9 (9.79 to 14.6)		
Serogroup Y (n=229,222)	49.8 (43.0 to 57.6)	36.1 (29.2 to 44.7)		
Serogroup W (n=229,222)	28.8 (24.6 to 33.7)	20.1 (16.7 to 24.2)		

Statistical analyses

Statistical analysis title	Serogroup A

Statistical analysis description:

Actual number of subjects analyzed = 449

Comparison groups	Group 1: MenACYW Conjugate Vaccine v Group 2: MENVEO® Vaccine
Number of subjects included in analysis	452
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT Ratio
Point estimate	1.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.883
upper limit	1.47

Statistical analysis title	Serogroup C
Comparison groups	Group 1: MenACYW Conjugate Vaccine v Group 2: MENVEO® Vaccine

Number of subjects included in analysis	452
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT Ratio
Point estimate	17.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.4
upper limit	22.6

Statistical analysis title	Serogroup Y
Statistical analysis description:	
Actual number of subjects analyzed = 451	
Comparison groups	Group 1: MenACYW Conjugate Vaccine v Group 2: MENVEO® Vaccine
Number of subjects included in analysis	452
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT Ratio
Point estimate	1.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.07
upper limit	1.78

Statistical analysis title	Serogroup W
Statistical analysis description:	
Actual number of subjects analyzed = 451	
Comparison groups	Group 1: MenACYW Conjugate Vaccine v Group 2: MENVEO® Vaccine
Number of subjects included in analysis	452
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT Ratio
Point estimate	1.43
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.12
upper limit	1.83

Secondary: GMTs of Meningococcal Serogroups A, C, Y, and W Antibodies Following

Vaccination With Either MenACYW Conjugate Vaccine or MENVEO® Vaccine in Children 6 to 9 Years of Age

End point title	GMTs of Meningococcal Serogroups A, C, Y, and W Antibodies Following Vaccination With Either MenACYW Conjugate Vaccine or MENVEO® Vaccine in Children 6 to 9 Years of Age

End point description:

Antibody titers against meningococcal serogroups A, C, Y, and W measured by hSBA. Analysis was performed on PPAS. Here 'Number of subjects analysed' signifies number of subjects in the PPAS aged 6-9 years, and 'n' signifies number of subjects with available data for specified category.

End point type	Secondary

End point timeframe:

Day 30 (post-vaccination)

End point values	Group 1: MenACYW Conjugate Vaccine	Group 2: MENVEO® Vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	229	237		
Units: titers				
geometric mean (confidence interval 95%)				
Serogroup A (n=228,237)	28.4 (23.9 to 33.8)	26.8 (22.0 to 32.6)		
Serogroup C (n=229,236)	272 (224 to 330)	23.7 (18.2 to 31.0)		
Serogroup Y (n=229,237)	95.1 (80.2 to 113)	51.8 (42.5 to 63.2)		
Serogroup W (n=229,237)	48.9 (42.5 to 56.3)	33.6 (28.2 to 40.1)		

Statistical analyses

Statistical analysis title	Serogroup A

Statistical analysis description:

Actual number of subjects analyzed = 465

Comparison groups	Group 1: MenACYW Conjugate Vaccine v Group 2: MENVEO® Vaccine
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT Ratio
Point estimate	1.06
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.816
upper limit	1.38

Statistical analysis title	Serogroup C
Statistical analysis description: Actual number of subjects analyzed = 465	
Comparison groups	Group 1: MenACYW Conjugate Vaccine v Group 2: MENVEO® Vaccine
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT Ratio
Point estimate	11.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.24
upper limit	16

Statistical analysis title	Serogroup Y
Comparison groups	Group 1: MenACYW Conjugate Vaccine v Group 2: MENVEO® Vaccine
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT Ratio
Point estimate	1.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.41
upper limit	2.38

Statistical analysis title	Serogroup W
Comparison groups	Group 1: MenACYW Conjugate Vaccine v Group 2: MENVEO® Vaccine
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT Ratio
Point estimate	1.45
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.16
upper limit	1.82

Secondary: Percentages of Subjects Achieving hSBA Vaccine Seroresponse for Meningococcal Serogroups A, C, Y, and W Following Vaccination With Either MenACYW Conjugate Vaccine or MENVEO® Vaccine in Children 2 to 5 Years of Age

End point title	Percentages of Subjects Achieving hSBA Vaccine Seroresponse for Meningococcal Serogroups A, C, Y, and W Following Vaccination With Either MenACYW Conjugate Vaccine or MENVEO® Vaccine in Children 2 to 5 Years of Age

End point description:

Antibody titers against meningococcal serogroups A, C, Y, and W measured by hSBA. The hSBA vaccine seroresponse for serogroups A, C, Y, and W was defined as post-vaccination hSBA titers >=1:16 for subjects with pre-vaccination hSBA titers <1:8 or at least a 4-fold increase in hSBA titers from pre- to post-vaccination for subjects with pre-vaccination hSBA titers >=1:8. Analysis was performed on PPAS. Here 'Number of subjects analysed' signifies number of subjects in the PPAS aged 2-5 years, and 'n' signifies number of subjects with available data for specified category.

End point type	Secondary

End point timeframe:

Day 30 (post-vaccination)

End point values	Group 1: MenACYW Conjugate Vaccine	Group 2: MENVEO® Vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	229	223		
Units: percentage of subjects				
number (confidence interval 95%)				
Serogroup A (n=227,221)	52.4 (45.7 to 59.1)	44.8 (38.1 to 51.6)		
Serogroup C (n=229,222)	94.3 (90.5 to 96.9)	43.2 (36.6 to 50.0)		
Serogroup Y (n=229,222)	88.2 (83.3 to 92.1)	77.0 (70.9 to 82.4)		
Serogroup W (n=229,222)	73.8 (67.6 to 79.4)	61.3 (54.5 to 67.7)		

Statistical analyses

Statistical analysis title	Serogroup A

Statistical analysis description:

Actual number of subjects analyzed = 448

Comparison groups	Group 1: MenACYW Conjugate Vaccine v Group 2: MENVEO® Vaccine

Number of subjects included in analysis	452
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	7.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	16.7

Statistical analysis title	Serogroup C
Statistical analysis description:	
Actual number of subjects analyzed = 451	
Comparison groups	Group 1: MenACYW Conjugate Vaccine v Group 2: MENVEO® Vaccine
Number of subjects included in analysis	452
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	51.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	43.5
upper limit	57.8

Statistical analysis title	Serogroup Y
Statistical analysis description:	
Actual number of subjects analyzed = 451	
Comparison groups	Group 1: MenACYW Conjugate Vaccine v Group 2: MENVEO® Vaccine
Number of subjects included in analysis	452
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	11.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.2
upper limit	18.1

Statistical analysis title	Serogroup W

Statistical analysis description:	
Actual number of subjects analyzed = 451	
Comparison groups	Group 1: MenACYW Conjugate Vaccine v Group 2: MENVEO® Vaccine
Number of subjects included in analysis	452
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	12.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.9
upper limit	20.9

Secondary: Percentages of Subjects Achieving hSBA Vaccine Seroresponse for Meningococcal Serogroups A, C, Y, and W Following Vaccination With Either MenACYW Conjugate Vaccine or MENVEO® Vaccine in Children 6 to 9 Years of Age

End point title	Percentages of Subjects Achieving hSBA Vaccine Seroresponse for Meningococcal Serogroups A, C, Y, and W Following Vaccination With Either MenACYW Conjugate Vaccine or MENVEO® Vaccine in Children 6 to 9 Years of Age

End point description:

Antibody titers against meningococcal serogroups A, C, Y, and W measured by hSBA. The hSBA vaccine seroresponse for serogroups A, C, Y, and W was defined as post-vaccination hSBA titers >=1:16 for subjects with pre-vaccination hSBA titers <1:8 or at least a 4-fold increase in hSBA titers from pre- to post-vaccination for subjects with pre-vaccination hSBA titers >=1:8. Analysis was performed on PPAS. Here 'Number of subjects analysed' signifies number of subjects in the PPAS aged 6-9 years, and 'n' signifies number of subjects with available data for specified category.

End point type	Secondary

End point timeframe:

Day 30 (post-vaccination)

End point values	Group 1: MenACYW Conjugate Vaccine	Group 2: MENVEO® Vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	229	237		
Units: percentage of subjects				
number (confidence interval 95%)				
Serogroup A (n=228,237)	58.3 (51.6 to 64.8)	50.6 (44.1 to 57.2)		
Serogroup C (n=229,236)	96.1 (92.7 to 98.2)	52.1 (45.5 to 58.6)		
Serogroup Y (n=229,237)	94.8 (91.0 to 97.3)	81.4 (75.9 to 86.2)		
Serogroup W (n=229,237)	83.8 (78.4 to 88.4)	66.7 (60.3 to 72.6)		

Statistical analyses

Statistical analysis title	Serogroup A
Statistical analysis description:	
Actual number of subjects analyzed = 465	
Comparison groups	Group 1: MenACYW Conjugate Vaccine v Group 2: MENVEO® Vaccine
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	7.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	16.6

Statistical analysis title	Serogroup C
Statistical analysis description:	
Actual number of subjects analyzed = 465	
Comparison groups	Group 1: MenACYW Conjugate Vaccine v Group 2: MENVEO® Vaccine
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	44
Confidence interval	
level	95 %
sides	2-sided
lower limit	36.8
upper limit	50.6

Statistical analysis title	Serogroup Y
Comparison groups	Group 1: MenACYW Conjugate Vaccine v Group 2: MENVEO® Vaccine

Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	13.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.6
upper limit	19.2

Statistical analysis title	Serogroup W
Comparison groups	Group 1: MenACYW Conjugate Vaccine v Group 2: MENVEO® Vaccine
Number of subjects included in analysis	466
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Percentage Difference
Point estimate	17.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	9.4
upper limit	24.7

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse event (AE) data were collected from Day 0 up to Day 30 post-vaccination. Solicited Reaction (SR) data were collected from Day 0 up to Day 7 post-vaccination.

Adverse event reporting additional description:

A SR was an AE that was prelisted (i.e.,solicited) in the electronic case report form (eCRF) and considered to be related to vaccination (adverse drug reaction). An unsolicited AE was an observed AE that did not fulfill the conditions prelisted in the eCRF (i.e.,solicited) in terms of symptom and/or onset post-vaccination. Safety analysis set.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Group 2: MENVEO® Vaccine

Reporting group description:

Healthy, meningococcal-vaccine naïve subjects aged 2 to 9 years received a single dose of MENVEO® vaccine.

Reporting group title	Group 1: MenACYW Conjugate Vaccine

Reporting group description:

Healthy, meningococcal-vaccine naïve subjects aged 2 to 9 years received a single dose of MenACYW conjugate vaccine.

Serious adverse events	Group 2: MENVEO® Vaccine	Group 1: MenACYW Conjugate Vaccine	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 494 (0.61%)	7 / 498 (1.41%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Vascular disorders			
Circulatory Collapse			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Partial Seizures			
subjects affected / exposed	1 / 494 (0.20%)	0 / 498 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tethered Cord Syndrome			

subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
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			
Adenoidal Hypertrophy			
subjects affected / exposed	1 / 494 (0.20%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	1 / 494 (0.20%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status Asthmaticus			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillar Hypertrophy			
subjects affected / exposed	1 / 494 (0.20%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wheezing			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Osteomyelitis			
subjects affected / exposed	0 / 494 (0.00%)	1 / 498 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Group 2: MENVEO® Vaccine	Group 1: MenACYW Conjugate Vaccine	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	335 / 494 (67.81%)	304 / 498 (61.04%)	
Nervous system disorders			
Headache			
subjects affected / exposed	60 / 494 (12.15%)	64 / 498 (12.85%)	
occurrences (all)	63	65	
General disorders and administration site conditions			
Injection Site Erythema			
subjects affected / exposed	153 / 494 (30.97%)	110 / 498 (22.09%)	
occurrences (all)	154	110	
Injection Site Pain			
subjects affected / exposed	206 / 494 (41.70%)	188 / 498 (37.75%)	
occurrences (all)	206	188	
Injection Site Swelling			
subjects affected / exposed	104 / 494 (21.05%)	67 / 498 (13.45%)	
occurrences (all)	105	67	
Malaise			
subjects affected / exposed	99 / 494 (20.04%)	103 / 498 (20.68%)	
occurrences (all)	99	103	
Pyrexia			
subjects affected / exposed	27 / 494 (5.47%)	20 / 498 (4.02%)	
occurrences (all)	27	21	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	30 / 494 (6.07%)	34 / 498 (6.83%)	
occurrences (all)	33	36	
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	112 / 494 (22.67%)	99 / 498 (19.88%)	
occurrences (all)	112	99	
Infections and infestations			
Pharyngitis			
subjects affected / exposed	25 / 494 (5.06%)	24 / 498 (4.82%)	
occurrences (all)	34	31	
Pharyngitis Streptococcal			

subjects affected / exposed	34 / 494 (6.88%)	18 / 498 (3.61%)	
occurrences (all)	38	23	
Upper Respiratory Tract Infection			
subjects affected / exposed	25 / 494 (5.06%)	20 / 498 (4.02%)	
occurrences (all)	30	24	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 August 2017	Following amendments were made- To accurately document the countries where the study was being conducted, Puerto Rico was added to different sections of the protocol as applicable. - Coordinating investigator information was added.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported