Clinical trial results:
Immunogenicity and Safety of an Investigational Quadrivalent Meningococcal Conjugate Vaccine in Toddlers 12 to 23 Months of Age

Summary

EudraCT number	2016-000749-30
Trial protocol	ES FI HU DE
Global end of trial date	26 October 2017

Results information

Result version number	v1 (current)
This version publication date	10 November 2018
First version publication date	10 November 2018

Trial information

Trial identification

Sponsor protocol code	MET51

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02955797
WHO universal trial number (UTN)	U1111-1161-2935

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	08 August 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 October 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

1) To demonstrate the non-inferiority of the antibody response to meningococcal serogroups A, C, Y, and W after a single dose of Meningococcal Polysaccharide (Serogroups A, C, Y and W) Tetanus Toxoid (MenACYW) conjugate vaccine or Nimenrix® in toddlers who either were meningococcal vaccine naïve or had received monovalent MenC vaccination during infancy
2) To demonstrate the non-inferiority of the antibody response to meningococcal serogroups A, C, Y, and W after a single dose of MenACYW conjugate vaccine or Nimenrix® in meningococcal vaccine naïve toddlers.

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 were also available on site in case of any immediate allergic reactions.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 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	Spain: 161
Country: Number of subjects enrolled	Finland: 356
Country: Number of subjects enrolled	Germany: 256
Country: Number of subjects enrolled	Hungary: 145
Worldwide total number of subjects	918
EEA total number of subjects	918

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	918

months)	
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:

Study subjects were enrolled in 34 centers in Spain, Hungary, Germany and Finland from 24 February to 21 September 2017.

Pre-assignment

Screening details:

A total of 918 subjects who met all inclusion and none of the exclusion criteria, including 5 subjects who did not meet all protocol-specified inclusion/exclusion criteria, were randomized and vaccinated in the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1(Meningococcal Vaccine-Naïve):MenACYW Conjugate Vaccine

Arm description:

Healthy, meningococcal C-vaccine naive toddlers aged 12 to 23 months 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

Arm title	Group 2 (Meningococcal Vaccine-Naïve): Nimenrix®

Arm description:

Healthy, meningococcal C-vaccine naive toddlers aged 12 to 23 months received a single dose of Nimenrix vaccine.

Arm type	Active comparator
Investigational medicinal product name	NIMENRIX®: Meningococcal group A, C, W-135 and Y conjugate vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 ml, intramuscular, single dose

Arm title	Group 3 (MenC-Primed): MenACYW Conjugate Vaccine

Arm description:

Healthy, meningococcal C-vaccine primed toddlers aged 12 to 23 months 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

Arm title	Group 4 (MenC-Primed): Nimenrix®

Arm description:

Healthy, meningococcal C-vaccine primed toddlers aged 12 to 23 months received a single dose of NIMENRIX® vaccine.

Arm type	Active comparator
Investigational medicinal product name	NIMENRIX®: Meningococcal group A, C, W-135 and Y Conjugate Vaccine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 ml, intramuscular, single dose

Number of subjects in period 1	Group 1(Meningococcal Vaccine-Naïve):MenACYW Conjugate Vaccine	Group 2 (Meningococcal Vaccine-Naïve): Nimenrix®	Group 3 (MenC-Primed): MenACYW Conjugate Vaccine
Started	306	306	203
Completed	303	303	203
Not completed	3	3	0
Consent withdrawn by subject	2	2	-
Lost to follow-up	-	1	-
Protocol deviation	1	-	-

Number of subjects in period 1	Group 4 (MenC-Primed): Nimenrix®
Started	103
Completed	101
Not completed	2
Consent withdrawn by subject	1
Lost to follow-up	-
Protocol deviation	1

Baseline characteristics

Reporting groups	
Reporting group title	Group 1(Meningococcal Vaccine-Naïve):MenACYW Conjugate Vaccine
Reporting group description:	
Healthy, meningococcal C-vaccine naive toddlers aged 12 to 23 months received a single dose of MenACYW conjugate vaccine.	
Reporting group title	Group 2 (Meningococcal Vaccine-Naïve): Nimenrix®
Reporting group description:	
Healthy, meningococcal C-vaccine naive toddlers aged 12 to 23 months received a single dose of Nimenrix vaccine.	
Reporting group title	Group 3 (MenC-Primed): MenACYW Conjugate Vaccine
Reporting group description:	
Healthy, meningococcal C-vaccine primed toddlers aged 12 to 23 months received a single dose of MenACYW conjugate vaccine.	
Reporting group title	Group 4 (MenC-Primed): Nimenrix®
Reporting group description:	
Healthy, meningococcal C-vaccine primed toddlers aged 12 to 23 months received a single dose of NIMENRIX® vaccine.	

Reporting group values	Group 1(Meningococcal Vaccine-Naïve):MenACYW Conjugate Vaccine	Group 2 (Meningococcal Vaccine-Naïve): Nimenrix®	Group 3 (MenC-Primed): MenACYW Conjugate Vaccine
Number of subjects	306	306	203
Age categorical			
Units: Subjects			
Age continuous			
Units: months			
arithmetic mean	16.1	16.2	14.0
standard deviation	± 3.32	± 3.19	± 3.01
Gender categorical			
Units: Subjects			
Female	140	145	97
Male	166	161	106

Reporting group values	Group 4 (MenC-Primed): Nimenrix®	Total	
Number of subjects	103	918	
Age categorical			
Units: Subjects			
Age continuous			
Units: months			
arithmetic mean	13.8		
standard deviation	± 2.72	-	
Gender categorical			
Units: Subjects			
Female	53	435	

Male	50	483	

End points

End points reporting groups

Reporting group title	Group 1(Meningococcal Vaccine-Naïve):MenACYW Conjugate Vaccine
Reporting group description:	
Healthy, meningococcal C-vaccine naive toddlers aged 12 to 23 months received a single dose of MenACYW conjugate vaccine.	
Reporting group title	Group 2 (Meningococcal Vaccine-Naïve): Nimenrix®
Reporting group description:	
Healthy, meningococcal C-vaccine naive toddlers aged 12 to 23 months received a single dose of Nimenrix vaccine.	
Reporting group title	Group 3 (MenC-Primed): MenACYW Conjugate Vaccine
Reporting group description:	
Healthy, meningococcal C-vaccine primed toddlers aged 12 to 23 months received a single dose of MenACYW conjugate vaccine.	
Reporting group title	Group 4 (MenC-Primed): Nimenrix®
Reporting group description:	
Healthy, meningococcal C-vaccine primed toddlers aged 12 to 23 months received a single dose of NIMENRIX® vaccine.	
Subject analysis set title	MenACYW (Group 1&3)
Subject analysis set type	Per protocol
Subject analysis set description:	
All meningococcal-vaccine naive and meningococcal-vaccine primed subjects who received a single dose of MenACYW conjugate vaccine.	
Subject analysis set title	Nimnerix (Group 2&4)
Subject analysis set type	Per protocol
Subject analysis set description:	
All meningococcal-vaccine naive and meningococcal-vaccine primed subjects who received a single dose of NIMENRIX® vaccine.	

Primary: Percentage of Subjects With Antibody Titers Greater Than or Equal to (>=) 1:8 Against Meningococcal Serogroups A, C, Y, and W in Toddlers who Either Were Meningococcal Vaccine Naïve or Had Received Monovalent MenC Vaccination During Infancy

End point title	Percentage of Subjects With Antibody Titers Greater Than or Equal to (>=) 1:8 Against Meningococcal Serogroups A, C, Y, and W in Toddlers who Either Were Meningococcal Vaccine Naïve or Had Received Monovalent MenC Vaccination During Infancy
End point description:	
Per-protocol analysis set was a subset of full analysis set which included all subjects who received at least 1 dose of the study vaccine and had a valid post-vaccination serology result. The subjects who presented protocol deviations were excluded from per-protocol analysis set. Here, "n" signified number of subjects with available data for each category.	
End point type	Primary
End point timeframe:	
Day 30 (post-vaccination)	

End point values	MenACYW (Group 1&3)	Nimnerix (Group 2&4)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	491	395		
Units: percentage of subjects				
number (confidence interval 95%)				
Serogroup A (n =490, 394)	90.4 (87.4 to 92.9)	91.6 (88.4 to 94.2)		
Serogroup C (n=489, 394)	99.2 (97.9 to 99.8)	85.5 (81.7 to 88.9)		
Serogroup Y (n=490, 395)	94.3 (91.8 to 96.2)	91.6 (88.5 to 94.2)		
Serogroup W (n=489, 394)	84.9 (81.4 to 87.9)	84.0 (80.0 to 87.5)		

Statistical analyses

Statistical analysis title	Serogroup A
Statistical analysis description:	
Actual number of subjects analyzed = 884	
Comparison groups	MenACYW (Group 1&3) v Nimnerix (Group 2&4)
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Difference (stratified)
Point estimate	-2.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.84
upper limit	1.78

Notes:

[1] - 95% confidence interval (CI) was stratified on the priming status (meningococcal vaccine naïve or primed monovalent MenC vaccination during infancy) and calculated using the Wald method (normal approximation). Weighted average of the difference over strata was calculated using the Minimal Risk weights with the null variance method. 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 = 883	
Comparison groups	MenACYW (Group 1&3) v Nimnerix (Group 2&4)
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Difference (stratified)
Point estimate	12.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	8.16
upper limit	16.1

Notes:

[2] - 95% CI was stratified on the priming status (meningococcal vaccine naïve or primed monovalent MenC vaccination during infancy) and calculated using the Wald method (normal approximation). Weighted average of the difference over strata was calculated using the Minimal Risk weights with the null variance method. Non-inferiority was demonstrated if the lower limit of the 2-sided 95% confidence interval (CI) of the difference between the 2 percentages was > -10%.

Statistical analysis title	Serogroup Y

Statistical analysis description:

Actual number of subjects analyzed = 885

Comparison groups	MenACYW (Group 1&3) v Nimnerix (Group 2&4)
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Difference (stratified)
Point estimate	2.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.34
upper limit	6.19

Notes:

[3] - 95% CI was stratified on the priming status (meningococcal vaccine naïve or primed monovalent MenC vaccination during infancy) and calculated using the Wald method (normal approximation). Weighted average of the difference over strata was calculated using the Minimal Risk weights with the null variance method. Non-inferiority was demonstrated if the lower limit of the 2-sided 95% confidence interval (CI) of the difference between the 2 percentages was > -10%.

Statistical analysis title	Serogroup W

Statistical analysis description:

Actual number of subjects analyzed = 883

Comparison groups	MenACYW (Group 1&3) v Nimnerix (Group 2&4)
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Parameter estimate	Difference (stratified)
Point estimate	0.458
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.37
upper limit	5.28

Notes:

[4] - 95% CI was stratified on the priming status (meningococcal vaccine naïve or primed monovalent MenC vaccination during infancy) and calculated using the Wald method (normal approximation). Weighted average of the difference over strata was calculated using the Minimal Risk weights with the null variance method. Non-inferiority was demonstrated if the lower limit of the 2-sided 95% confidence interval (CI) of the difference between the 2 percentages was > -10%.

Primary: Percentage of Subjects With Antibody Titers >= 1:8 Against Meningococcal Serogroups A, C, Y, and W in Meningococcal Vaccine Naïve Toddlers

End point title	Percentage of Subjects With Antibody Titers >= 1:8 Against Meningococcal Serogroups A, C, Y, and W in Meningococcal Vaccine Naïve Toddlers[5]

End point description:

Per-protocol analysis set was a subset of full analysis set which included all subjects who received at least 1 dose of the study vaccine and had a valid post-vaccination serology result. The subjects who

presented protocol deviations were excluded from per-protocol analysis set. Here, "n" signified number of subjects with available data for each category.

End point type	Primary

End point timeframe:

Day 30 (post-vaccination)

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: The statistical comparison was planned to be analysed for the reported arms only.

End point values	Group 1(Meningococcal Vaccine-Naïve):MenACYW Conjugate Vaccine	Group 2 (Meningococcal Vaccine-Naïve): Nimenrix®		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	293	296		
Units: percentage of subjects				
number (confidence interval 95%)				
Serogroup A (n =293, 295)	90.8 (86.9 to 93.8)	89.5 (85.4 to 92.7)		
Serogroup C (n=293, 295)	99.3 (97.6 to 99.9)	81.4 (76.4 to 85.6)		
Serogroup Y (n=293, 296)	93.2 (89.7 to 95.8)	91.6 (87.8 to 94.5)		
Serogroup W (n=293, 296)	83.6 (78.9 to 87.7)	83.4 (78.7 to 87.5)		

Statistical analyses

Statistical analysis title	Serogroup A

Statistical analysis description:

Actual number of subjects analyzed = 588

Comparison groups	Group 1(Meningococcal Vaccine-Naïve):MenACYW Conjugate Vaccine v Group 2 (Meningococcal Vaccine-Naïve): Nimenrix®
Number of subjects included in analysis	589
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
Parameter estimate	Difference in Percentage
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.6
upper limit	6.2

Notes:

[6] - 95% CI of the difference in percentages was computed using 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 = 588

Comparison groups	Group 1(Meningococcal Vaccine-Naïve):MenACYW Conjugate Vaccine v Group 2 (Meningococcal Vaccine-Naïve): Nimenrix®
Number of subjects included in analysis	589
Analysis specification	Pre-specified
Analysis type	non-inferiority
Parameter estimate	Difference in Percentage
Point estimate	18
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.6
upper limit	22.8

Statistical analysis title	Serogroup Y

Statistical analysis description:

Actual number of subjects analyzed = 589

Comparison groups	Group 1(Meningococcal Vaccine-Naïve):MenACYW Conjugate Vaccine v Group 2 (Meningococcal Vaccine-Naïve): Nimenrix®
Number of subjects included in analysis	589
Analysis specification	Pre-specified
Analysis type	non-inferiority[7]
Parameter estimate	Difference in Percentage
Point estimate	1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.76
upper limit	6.03

Notes:

[7] - 95% CI of the difference in percentages was computed using 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 = 589

Comparison groups	Group 1(Meningococcal Vaccine-Naïve):MenACYW Conjugate Vaccine v Group 2 (Meningococcal Vaccine-Naïve): Nimenrix®
Number of subjects included in analysis	589
Analysis specification	Pre-specified
Analysis type	non-inferiority[8]
Parameter estimate	Difference in Percentage
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.85
upper limit	6.18

Notes:

[8] - 95% CI of the difference in percentages was computed using 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) Against Meningococcal Serogroups A, C, Y, and W in Toddlers who Either Were Meningococcal Vaccine Naïve or Had Received Monovalent MenC Vaccination During Infancy

End point title	Geometric Mean Titers (GMTs) Against Meningococcal Serogroups A, C, Y, and W in Toddlers who Either Were Meningococcal Vaccine Naïve or Had Received Monovalent MenC Vaccination During Infancy

End point description:

Per-protocol analysis set was a subset of full analysis set which included all subjects who received at least 1 dose of the study vaccine and had a valid post-vaccination serology result. The subjects who presented protocol deviations were excluded from per-protocol analysis set. Here, "n" signified number of subjects with available data for each category.

End point type	Secondary

End point timeframe:

Day 30 (post-vaccination)

End point values	MenACYW (Group 1&3)	Nimnerix (Group 2&4)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	491	395		
Units: Titers				
number (not applicable)				
Serogroup A (n =490, 394)	29.9	34.5		
Serogroup C (n=489, 394)	880	77.1		
Serogroup Y (n=490, 395)	41.7	31.9		
Serogroup W (n=489, 394)	24.4	17.7		

Statistical analyses

Statistical analysis title	Serogroup A

Statistical analysis description:

Actual number of subjects analyzed = 884

Comparison groups	MenACYW (Group 1&3) v Nimnerix (Group 2&4)
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other[9]
Parameter estimate	GMT Ratio
Point estimate	0.819
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.697
upper limit	0.963

Notes:

[9] - 95% CI of the ratio of post-vaccination GMTs was stratified on the priming vaccination status (meningococcal vaccine naïve or primed monovalent MenC vaccination) and calculated using an analysis of variance (ANOVA) model of log10-transformed titers.

Statistical analysis title	Serogroup C
Statistical analysis description:	
Actual number of subjects analyzed = 883	
Comparison groups	MenACYW (Group 1&3) v Nimnerix (Group 2&4)
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other[10]
Parameter estimate	GMT Ratio
Point estimate	7.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	6.05
upper limit	9.52

Notes:

[10] - 95% CI of the ratio of post-vaccination GMTs was stratified on the priming vaccination status (meningococcal vaccine naïve or primed monovalent MenC vaccination) and calculated using an ANOVA model of log10-transformed titers.

Statistical analysis title	Serogroup Y
Statistical analysis description:	
Actual number of subjects analyzed = 885	
Comparison groups	MenACYW (Group 1&3) v Nimnerix (Group 2&4)
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other[11]
Parameter estimate	GMT Ratio
Point estimate	1.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.09
upper limit	1.51

Notes:

[11] - 95% CI of the ratio of post-vaccination GMTs was stratified on the priming vaccination status (meningococcal vaccine naïve or primed monovalent MenC vaccination) and calculated using an ANOVA model of log10-transformed titers.

Statistical analysis title	Serogroup W
Statistical analysis description:	
Actual number of subjects analyzed = 883	
Comparison groups	MenACYW (Group 1&3) v Nimnerix (Group 2&4)
Number of subjects included in analysis	886
Analysis specification	Pre-specified
Analysis type	other[12]
Parameter estimate	GMT Ratio
Point estimate	1.32

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.12
upper limit	1.56

Notes:

[12] - 95% CI of the ratio of post-vaccination GMTs was stratified on the priming vaccination status (meningococcal vaccine naïve or primed monovalent MenC vaccination) and calculated using an ANOVA model of log10-transformed titers.

Secondary: Geometric Mean Titers (GMTs) Against Meningococcal Serogroups A, C, Y, and W in Vaccine Naïve Toddlers

End point title	Geometric Mean Titers (GMTs) Against Meningococcal Serogroups A, C, Y, and W in Vaccine Naïve Toddlers[13]

End point description:

Per-protocol analysis set was a subset of full analysis set which included all subjects who received at least 1 dose of the study vaccine and had a valid post-vaccination serology result. The subjects who presented protocol deviations were excluded from per-protocol analysis set. Here, "n" signified number of subjects with available data for each category.

End point type	Secondary

End point timeframe:

Day 30 (post-vaccination)

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: The statistical comparison was planned to be be analysed for the reported arms only.

End point values	Group 1(Meningococcal Vaccine-Naïve):MenACYW Conjugate Vaccine	Group 2 (Meningococcal Vaccine-Naïve): Nimenrix®		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	293	296		
Units: Titers				
number (not applicable)				
Serogroup A (n =293, 295)	28.7	28.0		
Serogroup C (n =293, 295)	436	26.4		
Serogroup Y (n =293, 296)	38.0	32.2		
Serogroup W (n =293, 296)	22.0	16.4		

Statistical analyses

Statistical analysis title	Serogroup A

Statistical analysis description:

Actual number of subjects analyzed = 588

Comparison groups	Group 1(Meningococcal Vaccine-Naïve):MenACYW Conjugate Vaccine v Group 2 (Meningococcal Vaccine-Naïve): Nimenrix®

Number of subjects included in analysis	589
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT Ratio
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.24

Statistical analysis title	Serogroup C
Statistical analysis description:	
Actual number of subjects analyzed = 588	
Comparison groups	Group 1(Meningococcal Vaccine-Naïve):MenACYW Conjugate Vaccine v Group 2 (Meningococcal Vaccine-Naïve): Nimenrix®
Number of subjects included in analysis	589
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT Ratio
Point estimate	16.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	13.4
upper limit	20.4

Statistical analysis title	Serogroup Y
Comparison groups	Group 1(Meningococcal Vaccine-Naïve):MenACYW Conjugate Vaccine v Group 2 (Meningococcal Vaccine-Naïve): Nimenrix®
Number of subjects included in analysis	589
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT Ratio
Point estimate	1.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.97
upper limit	1.44

Statistical analysis title	Serogroup W
Comparison groups	Group 1(Meningococcal Vaccine-Naïve):MenACYW Conjugate Vaccine v Group 2 (Meningococcal Vaccine-Naïve): Nimenrix®

Number of subjects included in analysis	589
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT Ratio
Point estimate	1.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.1
upper limit	1.63

Secondary: Geometric Mean Titers (GMTs) Against Meningococcal Serogroups A, C, Y, and W in Toddlers who Had Received Monovalent MenC Vaccination During Infancy

End point title	Geometric Mean Titers (GMTs) Against Meningococcal Serogroups A, C, Y, and W in Toddlers who Had Received Monovalent MenC Vaccination During Infancy[14]

End point description:

Per-protocol analysis set was a subset of full analysis set which included all subjects who received at least 1 dose of the study vaccine and had a valid post-vaccination serology result. The subjects who presented protocol deviations were excluded from per-protocol analysis set. Here, "n" signified number of subjects with available data for each category.

End point type	Secondary

End point timeframe:

Day 30 (post-vaccination)

Notes:

[14] - 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: The statistical comparison was planned to be be analysed for the reported arms only.

End point values	Group 3 (MenC-Primed): MenACYW Conjugate Vaccine	Group 4 (MenC-Primed): Nimenrix®		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	198	99		
Units: Titers				
number (not applicable)				
Serogroup A (n =197, 99)	31.8	64.0		
Serogroup C (n =196, 99)	2514	1883		
Serogroup Y (n =197, 99)	48.0	31.3		
Serogroup W (n =196, 98)	28.7	22.3		

Statistical analyses

Statistical analysis title	Serogroup A

Statistical analysis description:

Actual number of subjects analyzed = 296

Comparison groups	Group 3 (MenC-Primed): MenACYW Conjugate Vaccine v Group 4 (MenC-Primed): Nimenrix®
Number of subjects included in analysis	297
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT Ratio
Point estimate	0.496
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.367
upper limit	0.672

Statistical analysis title	Serogroup C

Statistical analysis description:

Actual number of subjects analyzed = 295

Comparison groups	Group 3 (MenC-Primed): MenACYW Conjugate Vaccine v Group 4 (MenC-Primed): Nimenrix®
Number of subjects included in analysis	297
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT Ratio
Point estimate	1.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.814
upper limit	2.19

Statistical analysis title	Serogroup Y

Statistical analysis description:

Actual number of subjects analyzed = 296

Comparison groups	Group 3 (MenC-Primed): MenACYW Conjugate Vaccine v Group 4 (MenC-Primed): Nimenrix®
Number of subjects included in analysis	297
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT Ratio
Point estimate	1.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.15
upper limit	2.04

Statistical analysis title	Serogroup W
Statistical analysis description: Actual number of subjects analyzed = 294	
Comparison groups	Group 3 (MenC-Primed): MenACYW Conjugate Vaccine v Group 4 (MenC-Primed): Nimenrix®
Number of subjects included in analysis	297
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMT Ratio
Point estimate	1.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.944
upper limit	1.75

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:

SR was an AE that was prelisted in eCRF and considered to be related to vaccination. SR: adverse drug reaction observed and reported under the conditions prelisted (i.e., solicited) in eCRF. Unsolicited AE was an observed AE that did not fulfill conditions prelisted in eCRF 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 1: MenACYW conjugate vaccine - Naive

Reporting group description:

Healthy, meningococcal-vaccine naive toddlers aged 12 to 23 months received a single dose of MenACYW conjugate vaccine.

Reporting group title	Group 2: Nimenrix® - Naive

Reporting group description:

Healthy, meningococcal-vaccine naive toddlers aged 12 to 23 months received a single dose of NIMENRIX® vaccine.

Reporting group title	Group 3: MenACYW conjugate vaccine - MenC primed

Reporting group description:

Healthy, meningococcal C-vaccine primed toddlers aged 12 to 23 months received a single dose of MenACYW conjugate vaccine.

Reporting group title	Group 4: Nimenrix® - MenC primed

Reporting group description:

Healthy, meningococcal C-vaccine primed toddlers aged 12 to 23 months received a single dose of NIMENRIX® vaccine.

Serious adverse events	Group 1: MenACYW conjugate vaccine - Naive	Group 2: Nimenrix® - Naive	Group 3: MenACYW conjugate vaccine - MenC primed
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 303 (0.66%)	1 / 306 (0.33%)	2 / 203 (0.99%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
Blood Immunoglobulin A Decreased			
subjects affected / exposed	0 / 303 (0.00%)	0 / 306 (0.00%)	0 / 203 (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			

Contusion			
subjects affected / exposed	0 / 303 (0.00%)	1 / 306 (0.33%)	0 / 203 (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
Craniocerebral Injury			
subjects affected / exposed	0 / 303 (0.00%)	0 / 306 (0.00%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Intestinal Malrotation			
subjects affected / exposed	1 / 303 (0.33%)	0 / 306 (0.00%)	0 / 203 (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
Nervous system disorders			
Febrile Convulsion			
subjects affected / exposed	1 / 303 (0.33%)	0 / 306 (0.00%)	0 / 203 (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
Seizure			
subjects affected / exposed	0 / 303 (0.00%)	0 / 306 (0.00%)	1 / 203 (0.49%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Haemolytic Uraemic Syndrome			
subjects affected / exposed	1 / 303 (0.33%)	0 / 306 (0.00%)	0 / 203 (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
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	0 / 303 (0.00%)	0 / 306 (0.00%)	0 / 203 (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			
Bronchitis			

subjects affected / exposed	0 / 303 (0.00%)	0 / 306 (0.00%)	0 / 203 (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
Campylobacter Gastroenteritis			
subjects affected / exposed	0 / 303 (0.00%)	0 / 306 (0.00%)	1 / 203 (0.49%)
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 Escherichia Coli			
subjects affected / exposed	1 / 303 (0.33%)	0 / 306 (0.00%)	0 / 203 (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

Serious adverse events	Group 4: Nimenrix® - MenC primed		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 102 (1.96%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Investigations			
Blood Immunoglobulin A Decreased			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 102 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Craniocerebral Injury			
subjects affected / exposed	0 / 102 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Congenital, familial and genetic disorders			
Intestinal Malrotation			

subjects affected / exposed	0 / 102 (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	0 / 102 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Seizure			
subjects affected / exposed	0 / 102 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Haemolytic Uraemic Syndrome			
subjects affected / exposed	0 / 102 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Bronchospasm			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 102 (0.98%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Campylobacter Gastroenteritis			
subjects affected / exposed	0 / 102 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis Escherichia Coli			

subjects affected / exposed	0 / 102 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Group 1: MenACYW conjugate vaccine - Naive	Group 2: Nimenrix® - Naive	Group 3: MenACYW conjugate vaccine - MenC primed
Total subjects affected by non-serious adverse events			
subjects affected / exposed	261 / 303 (86.14%)	266 / 306 (86.93%)	151 / 203 (74.38%)
Nervous system disorders			
Somnolence			
subjects affected / exposed	64 / 303 (21.12%)	55 / 306 (17.97%)	51 / 203 (25.12%)
occurrences (all)	64	55	51
General disorders and administration site conditions			
Crying			
subjects affected / exposed	106 / 303 (34.98%)	111 / 306 (36.27%)	48 / 203 (23.65%)
occurrences (all)	109	112	48
Injection Site Erythema			
subjects affected / exposed	122 / 303 (40.26%)	116 / 306 (37.91%)	52 / 203 (25.62%)
occurrences (all)	123	116	52
Injection Site Pain			
subjects affected / exposed	122 / 303 (40.26%)	113 / 306 (36.93%)	55 / 203 (27.09%)
occurrences (all)	122	113	55
Injection Site Swelling			
subjects affected / exposed	63 / 303 (20.79%)	52 / 306 (16.99%)	35 / 203 (17.24%)
occurrences (all)	63	52	35
Pyrexia			
subjects affected / exposed	40 / 303 (13.20%)	48 / 306 (15.69%)	29 / 203 (14.29%)
occurrences (all)	42	48	29
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	23 / 303 (7.59%)	16 / 306 (5.23%)	8 / 203 (3.94%)
occurrences (all)	23	16	8
Teething			

subjects affected / exposed	16 / 303 (5.28%)	13 / 306 (4.25%)	12 / 203 (5.91%)
occurrences (all)	18	19	15
Vomiting			
subjects affected / exposed	23 / 303 (7.59%)	13 / 306 (4.25%)	21 / 203 (10.34%)
occurrences (all)	24	13	21
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	11 / 303 (3.63%)	13 / 306 (4.25%)	13 / 203 (6.40%)
occurrences (all)	11	16	13
Psychiatric disorders			
Irritability			
subjects affected / exposed	144 / 303 (47.52%)	127 / 306 (41.50%)	76 / 203 (37.44%)
occurrences (all)	145	128	76
Infections and infestations			
Bronchitis			
subjects affected / exposed	3 / 303 (0.99%)	2 / 306 (0.65%)	11 / 203 (5.42%)
occurrences (all)	4	2	11
Nasopharyngitis			
subjects affected / exposed	15 / 303 (4.95%)	18 / 306 (5.88%)	2 / 203 (0.99%)
occurrences (all)	19	18	2
Rhinitis			
subjects affected / exposed	21 / 303 (6.93%)	25 / 306 (8.17%)	5 / 203 (2.46%)
occurrences (all)	22	27	5
Upper Respiratory Tract Infection			
subjects affected / exposed	49 / 303 (16.17%)	39 / 306 (12.75%)	14 / 203 (6.90%)
occurrences (all)	55	43	14
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	91 / 303 (30.03%)	94 / 306 (30.72%)	56 / 203 (27.59%)
occurrences (all)	93	94	56

Non-serious adverse events	Group 4: Nimenrix® - MenC primed		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	65 / 102 (63.73%)		
Nervous system disorders			
Somnolence			

subjects affected / exposed	19 / 102 (18.63%)		
occurrences (all)	19		
General disorders and administration site conditions			
Crying			
subjects affected / exposed	23 / 102 (22.55%)		
occurrences (all)	23		
Injection Site Erythema			
subjects affected / exposed	21 / 102 (20.59%)		
occurrences (all)	21		
Injection Site Pain			
subjects affected / exposed	20 / 102 (19.61%)		
occurrences (all)	21		
Injection Site Swelling			
subjects affected / exposed	9 / 102 (8.82%)		
occurrences (all)	9		
Pyrexia			
subjects affected / exposed	14 / 102 (13.73%)		
occurrences (all)	15		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	4 / 102 (3.92%)		
occurrences (all)	4		
Teething			
subjects affected / exposed	6 / 102 (5.88%)		
occurrences (all)	7		
Vomiting			
subjects affected / exposed	8 / 102 (7.84%)		
occurrences (all)	8		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	5 / 102 (4.90%)		
occurrences (all)	5		
Psychiatric disorders			
Irritability			
subjects affected / exposed	36 / 102 (35.29%)		
occurrences (all)	36		

Infections and infestations Bronchitis subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all) Rhinitis subjects affected / exposed occurrences (all) Upper Respiratory Tract Infection subjects affected / exposed occurrences (all)	 1 / 102 (0.98%) 1 0 / 102 (0.00%) 0 0 / 102 (0.00%) 0 7 / 102 (6.86%) 8		
Metabolism and nutrition disorders Decreased Appetite subjects affected / exposed occurrences (all)	 28 / 102 (27.45%) 28		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported