Clinical trial results:
Immunogenicity and Safety of an Investigational Quadrivalent Meningococcal Conjugate Vaccine Versus Nimenrix® or NeisVac-C® in Healthy Toddlers 12 to 23 Months of Age

Summary

EudraCT number	2018-003790-10
Trial protocol	DK DE FI
Global end of trial date	14 October 2020

Results information

Result version number	v1
This version publication date	28 June 2021
First version publication date	28 June 2021

Trial information

Trial identification

Sponsor protocol code	MEQ00065

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03890367
WHO universal trial number (UTN)	U1111-1217-2456

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur
Sponsor organisation address	14 Espace Henry Vallée, Lyon, France, 69007
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)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	04 May 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	14 October 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Sequential approach: To demonstrate for serogroup C: - the non-inferiority of the hSBA seroprotection rate (titers>= 1:8) after MenACYW conjugate or Nimenrix® vaccination. If this non-inferiority was demonstrated, then to demonstrate - the non-inferiority in terms of GMT. If this non-inferiority was demonstrated, then to demonstrate - the superiority in terms of GMT. If this superiority was demonstrated, then to demonstrate - the superiority of the seroprotection rate or to demonstrate for serogroup C: - the non-inferiority of the rSBA seroprotection rate after MenACYW conjugate or NeisVac-C® vaccination. If this non-inferiority was demonstrated, then to demonstrate - the non-inferiority in terms of GMT. If this non-inferiority was demonstrated, then to demonstrate - the superiority in terms of GMT. The primary objective will be met if the non-inferiority of the hSBA seroprotection rate versus Nimenrix® or the non-inferiority of rSBA seroprotection rate versus NeisVac-C® was met.

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	12 September 2019
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	Denmark: 108
Country: Number of subjects enrolled	Finland: 313
Country: Number of subjects enrolled	Germany: 286
Worldwide total number of subjects	707
EEA total number of subjects	707

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)	707
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 29 active centers in Denmark, Germany and Finland from 12 September 2019 to 03 September 2020.

Pre-assignment

Screening details:

A total of 707 subjects were enrolled and randomised 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, Data analyst, Assessor

Blinding implementation details:

The study has a modified double-blind design that is the study contained an unblinded vaccine administrator while the rest of the study team, including laboratory technicians in charge of executing the serological testing, remained blinded to the subjects' group allocations throughout the study.

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1: MenACYW Conjugate Vaccine

Arm description:

Healthy, toddlers aged 12 to 23 months received a single dose of MenACYW Conjugate vaccine on Day 0.

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

Dosage and administration details:

0.5 milliliters (mL), intramuscular, single dose.

Arm title	Group 2: Nimenrix® Vaccine

Arm description:

Healthy, toddlers aged 12 to 23 months received a single dose of Nimenrix vaccine on Day 0.

Arm type	Active comparator
Investigational medicinal product name	Meningococcal group A, C, W-135 and Y Conjugate Vaccine
Investigational medicinal product code	
Other name	NIMENRIX®
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: NeisVac-C® Vaccine

Arm description:

Healthy, toddlers aged 12 to 23 months received a single dose of NeisVac-C vaccine on Day 0.

Arm type	Active comparator

Investigational medicinal product name	Meningococcal Group C Polysaccharide Conjugate Vaccine Adsorbed
Investigational medicinal product code	
Other name	NeisVac-C®
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

0.5 mL, intramuscular, single dose.

Number of subjects in period 1	Group 1: MenACYW Conjugate Vaccine	Group 2: Nimenrix® Vaccine	Group 3: NeisVac-C® Vaccine
Started	232	235	240
Safety Analysis Set	230	232	239
Completed	228	229	239
Not completed	4	6	1
Lost to follow-up	1	1	-
Withdrawal by parent/guardian	1	3	-
Protocol deviation	2	2	1

Baseline characteristics

Reporting groups	
Reporting group title	Group 1: MenACYW Conjugate Vaccine
Reporting group description:	
Healthy, toddlers aged 12 to 23 months received a single dose of MenACYW Conjugate vaccine on Day 0.	
Reporting group title	Group 2: Nimenrix® Vaccine
Reporting group description:	
Healthy, toddlers aged 12 to 23 months received a single dose of Nimenrix vaccine on Day 0.	
Reporting group title	Group 3: NeisVac-C® Vaccine
Reporting group description:	
Healthy, toddlers aged 12 to 23 months received a single dose of NeisVac-C vaccine on Day 0.	

Reporting group values	Group 1: MenACYW Conjugate Vaccine	Group 2: Nimenrix® Vaccine	Group 3: NeisVac-C® Vaccine
Number of subjects	232	235	240
Age categorical			
Units: Subjects			
Age continuous			
Units: months			
arithmetic mean	16.5	16.6	16.7
standard deviation	± 3.27	± 3.48	± 3.45
Gender categorical			
Units: Subjects			
Female	115	108	109
Male	117	127	131
Race			
Units: Subjects			
American Indian or Alaska Native	0	1	0
Asian	1	2	1
Black or African American	2	0	1
Native Hawaiian or Other Pacific Islander	0	0	0
White	225	226	236
Mixed origin	3	5	1
Not Reported	0	0	0
Unknown	1	1	1

Reporting group values	Total		
Number of subjects	707		
Age categorical			
Units: Subjects			
Age continuous			
Units: months			
arithmetic mean			
standard deviation	-		

Gender categorical Units: Subjects			
Female	332		
Male	375		
Race Units: Subjects			
American Indian or Alaska Native	1		
Asian	4		
Black or African American	3		
Native Hawaiian or Other Pacific Islander	0		
White	687		
Mixed origin	9		
Not Reported	0		
Unknown	3		

End points

End points reporting groups

Reporting group title	Group 1: MenACYW Conjugate Vaccine
Reporting group description:	
Healthy, toddlers aged 12 to 23 months received a single dose of MenACYW Conjugate vaccine on Day 0.	
Reporting group title	Group 2: Nimenrix® Vaccine
Reporting group description:	
Healthy, toddlers aged 12 to 23 months received a single dose of Nimenrix vaccine on Day 0.	
Reporting group title	Group 3: NeisVac-C® Vaccine
Reporting group description:	
Healthy, toddlers aged 12 to 23 months received a single dose of NeisVac-C vaccine on Day 0.	

Primary: Percentage of Subjects With Antibody Titers >=1:8 Against Meningococcal Serogroup C Measured by Serum Bactericidal Assay Using Human Complement (hSBA) Following Vaccination with MenACYW Conjugate Vaccine or Nimenrix® (Non-inferiority Analysis)

End point title	Percentage of Subjects With Antibody Titers >=1:8 Against Meningococcal Serogroup C Measured by Serum Bactericidal Assay Using Human Complement (hSBA) Following Vaccination with MenACYW Conjugate Vaccine or Nimenrix® (Non-inferiority Analysis)[1]
End point description:	
Antibody titers against Meningococcal Serogroup C were measured by hSBA. Analysis was performed on hSBA per-protocol analysis set (PPAS) which was a subset that 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 PPAS.	
End point type	Primary
End point timeframe:	
Day 30 (post-vaccination)	

Notes:

[1] - 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: Data was planned to be collected and analysed for Group 1 and Group 2 only, as pre-specified in protocol.

End point values	Group 1: MenACYW Conjugate Vaccine	Group 2: Nimenrix® Vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	214	211		
Units: percentage of subjects				
number (confidence interval 95%)	99.5 (97.4 to 100)	89.1 (84.1 to 93.0)		

Statistical analyses

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

	Vaccine
Number of subjects included in analysis	425
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Difference in Percentage
Point estimate	10.43
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	5.68
upper limit	16.2

Notes:

[2] - The two-sided 97.5 percent (%) confidence interval (CI) was calculated based on the Wilson score method without continuity correction. The non-inferiority was demonstrated if the lower limit of the 97.5% CI of the percentage difference between compared groups was greater than (>) -10%.

Primary: Geometric Mean Titers (GMTs) of Antibodies Against Meningococcal Serogroup C Measured by hSBA Following Vaccination with MenACYW Conjugate Vaccine or Nimenrix® (Non-inferiority Analysis)

End point title	Geometric Mean Titers (GMTs) of Antibodies Against Meningococcal Serogroup C Measured by hSBA Following Vaccination with MenACYW Conjugate Vaccine or Nimenrix® (Non-inferiority Analysis)[3]

End point description:

GMT titers against Meningococcal Serogroup C were measured by hSBA. Titers were expressed in terms of 1/dilution. Analysis was performed on hSBA PPAS which was a subset that 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 PPAS.

End point type	Primary

End point timeframe:

Day 30 (post-vaccination)

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: Data was planned to be collected and analysed for Group 1 and Group 2 only, as pre-specified in protocol.

End point values	Group 1: MenACYW Conjugate Vaccine	Group 2: Nimenrix® Vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	214	211		
Units: titers				
geometric mean (confidence interval 95%)	515 (450 to 591)	31.6 (26.5 to 37.6)		

Statistical analyses

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

Number of subjects included in analysis	425
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Parameter estimate	GMT Ratio
Point estimate	16.3
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	12.7
upper limit	21

Notes:

[4] - The two-sided 97.5% CI of the ratio of post-vaccination GMTs was calculated using normal approximation of log-transformed titers. The non-inferiority was demonstrated if the lower limit of the two-sided 97.5% CI of the ratio of GMTs between compared groups was >1/1.5.

Primary: GMTs of Antibodies Against Meningococcal Serogroup C Measured by hSBA Following Vaccination with MenACYW Conjugate Vaccine or Nimenrix® (Superiority Analysis)

End point title	GMTs of Antibodies Against Meningococcal Serogroup C Measured by hSBA Following Vaccination with MenACYW Conjugate Vaccine or Nimenrix® (Superiority Analysis)[5]

End point description:

GMT titers against Meningococcal Serogroup C were measured by hSBA. Titers were expressed in terms of 1/dilution. Analysis was performed on hSBA PPAS which was a subset that 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 PPAS.

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: Data was planned to be collected and analysed for Group 1 and Group 2 only, as pre-specified in protocol.

End point values	Group 1: MenACYW Conjugate Vaccine	Group 2: Nimenrix® Vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	214	211		
Units: titers				
geometric mean (confidence interval 95%)	515 (450 to 591)	31.6 (26.5 to 37.6)		

Statistical analyses

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

Number of subjects included in analysis	425
Analysis specification	Pre-specified
Analysis type	superiority[6]
Parameter estimate	GMT Ratio
Point estimate	16.3
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	12.7
upper limit	21

Notes:

[6] - The two-sided 97.5% CI of the ratio of post-vaccination GMTs was calculated using normal approximation of log-transformed titers. The superiority was demonstrated if the lower limit of the two-sided 97.5% CI of the ratio of GMTs between compared groups was >1.

Primary: Percentage of Subjects With Antibody Titers >=1:8 Against Meningococcal Serogroup C Measured by hSBA Following Vaccination with MenACYW Conjugate Vaccine or Nimenrix® (Superiority Analysis)

End point title	Percentage of Subjects With Antibody Titers >=1:8 Against Meningococcal Serogroup C Measured by hSBA Following Vaccination with MenACYW Conjugate Vaccine or Nimenrix® (Superiority Analysis)[7]

End point description:

Antibody titers against Meningococcal Serogroup C were measured by hSBA. Analysis was performed on hSBA PPAS which was a subset that 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 PPAS.

End point type	Primary

End point timeframe:

Day 30 (post-vaccination)

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: Data was planned to be collected and analysed for Group 1 and Group 2 only, as pre-specified in protocol.

End point values	Group 1: MenACYW Conjugate Vaccine	Group 2: Nimenrix® Vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	214	211		
Units: percentage of subjects				
number (confidence interval 95%)	99.5 (97.4 to 100)	89.1 (84.1 to 93.0)		

Statistical analyses

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

Number of subjects included in analysis	425
Analysis specification	Pre-specified
Analysis type	superiority[8]
Parameter estimate	Difference in Percentage
Point estimate	10.43
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	5.68
upper limit	16.2

Notes:

[8] - The two-sided 97.5% CI was calculated based on the Wilson score method without continuity correction. The superiority was demonstrated if the lower limit of the 97.5% CI of the percentage difference between compared groups was >0%.

Primary: Percentage of Subjects With Antibody Titers >=1:8 Against Meningococcal Serogroup C Measured by Serum Bactericidal Assay Using Baby Rabbit Complement (rSBA) Following Vaccination with MenACYW Conjugate Vaccine or NeisVac-C (Non-inferiority Analysis)

End point title	Percentage of Subjects With Antibody Titers >=1:8 Against Meningococcal Serogroup C Measured by Serum Bactericidal Assay Using Baby Rabbit Complement (rSBA) Following Vaccination with MenACYW Conjugate Vaccine or NeisVac-C (Non-inferiority Analysis)[9]

End point description:

Antibody titers against Meningococcal Serogroup C were measured by rSBA. Analysis was performed on rSBA PPAS which was a subset that 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 PPAS.

End point type	Primary

End point timeframe:

Day 30 (post-vaccination)

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: Data was planned to be collected and analysed for Group 1 and Group 3 only, as pre-specified in protocol.

End point values	Group 1: MenACYW Conjugate Vaccine	Group 3: NeisVac-C® Vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	213	215		
Units: percentage of subjects				
number (confidence interval 95%)	100 (98.3 to 100)	100 (98.3 to 100)		

Statistical analyses

Statistical analysis title	MenACYW Conjugate Vaccine, NeisVac-C®: Serogroup C
Comparison groups	Group 1: MenACYW Conjugate Vaccine v Group 3: NeisVac-C® Vaccine

Number of subjects included in analysis	428
Analysis specification	Pre-specified
Analysis type	non-inferiority[10]
Parameter estimate	Difference in Percentage
Point estimate	0
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-2.3
upper limit	2.28

Notes:

[10] - The two-sided 97.5% CI was calculated based on the Wilson score method without continuity correction. The non-inferiority was demonstrated if the lower limit of the 97.5% CI of the percentage difference between compared groups was >-10%.

Primary: GMTs of Antibodies against Meningococcal Serogroup C Measured by rSBA Following Vaccination with MenACYW Conjugate Vaccine or NeisVac-C® (Non-inferiority Analysis)

End point title	GMTs of Antibodies against Meningococcal Serogroup C Measured by rSBA Following Vaccination with MenACYW Conjugate Vaccine or NeisVac-C® (Non-inferiority Analysis)[11]

End point description:

GMT titers against Meningococcal Serogroup C were measured by rSBA. Titers were expressed in terms of 1/dilution. Analysis was performed on rSBA PPAS which was a subset that 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 PPAS.

End point type	Primary

End point timeframe:

Day 30 (post-vaccination)

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: Data was planned to be collected and analysed for Group 1 and Group 3 only, as pre-specified in protocol.

End point values	Group 1: MenACYW Conjugate Vaccine	Group 3: NeisVac-C® Vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	213	215		
Units: titers				
geometric mean (confidence interval 95%)	2143 (1870 to 2456)	1624 (1425 to 1850)		

Statistical analyses

Statistical analysis title	MenACYW Conjugate Vaccine, NeisVac-C®: Serogroup C
Comparison groups	Group 1: MenACYW Conjugate Vaccine v Group 3: NeisVac-C® Vaccine

Number of subjects included in analysis	428
Analysis specification	Pre-specified
Analysis type	non-inferiority[12]
Parameter estimate	GMT Ratio
Point estimate	1.32
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.06
upper limit	1.64

Notes:

[12] - The two-sided 97.5% CI of the ratio of post-vaccination GMTs was calculated using normal approximation of log-transformed titers. The non-inferiority was demonstrated if the lower limit of the two-sided 97.5% CI of the ratio of GMTs between compared groups was > 1/1.5.

Primary: GMTs of Antibodies against Meningococcal Serogroup C Measured by rSBA Following Vaccination with MenACYW Conjugate Vaccine or NeisVac-C® (Superiority Analysis)

End point title	GMTs of Antibodies against Meningococcal Serogroup C Measured by rSBA Following Vaccination with MenACYW Conjugate Vaccine or NeisVac-C® (Superiority Analysis)[13]

End point description:

GMT titers against Meningococcal Serogroup C were measured by rSBA. Titers were expressed in terms of 1/dilution. Analysis was performed on rsBA PPAS which was a subset that 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 PPAS.

End point type	Primary

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: Data was planned to be collected and analysed for Group 1 and Group 3 only, as pre-specified in protocol.

End point values	Group 1: MenACYW Conjugate Vaccine	Group 3: NeisVac-C® Vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	213	215		
Units: titers				
geometric mean (confidence interval 95%)	2143 (1870 to 2456)	1624 (1425 to 1850)		

Statistical analyses

Statistical analysis title	MenACYW Conjugate Vaccine, NeisVac-C®: Serogroup C
Comparison groups	Group 1: MenACYW Conjugate Vaccine v Group 3: NeisVac-C® Vaccine

Number of subjects included in analysis	428
Analysis specification	Pre-specified
Analysis type	superiority[14]
Parameter estimate	GMT Ratio
Point estimate	1.32
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.06
upper limit	1.64

Notes:

[14] - The two-sided 97.5% CI of the ratio of post-vaccination GMTs was calculated using normal approximation of log-transformed titers. The superiority was demonstrated if the lower limit of the two-sided 97.5% CI of the ratio of GMTs between compared groups was >1.

Secondary: Percentage of Subjects With Antibody Titers >=1:8 Against Meningococcal Serogroup C Measured by rSBA Following Vaccination with MenACYW Conjugate Vaccine or Nimenrix® (Non-inferiority Analysis)

End point title	Percentage of Subjects With Antibody Titers >=1:8 Against Meningococcal Serogroup C Measured by rSBA Following Vaccination with MenACYW Conjugate Vaccine or Nimenrix® (Non-inferiority Analysis)[15]

End point description:

Antibody titers against Meningococcal Serogroup C were measured by rSBA. Analysis was performed on rSBA PPAS which was a subset that 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 PPAS.

End point type	Secondary

End point timeframe:

Day 30 (post-vaccination)

Notes:

[15] - 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: Data was planned to be collected and analysed for Group 1 and Group 2 only, as pre-specified in protocol.

End point values	Group 1: MenACYW Conjugate Vaccine	Group 2: Nimenrix® Vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	213	210		
Units: percentage of subjects				
number (confidence interval 95%)	100 (98.3 to 100)	94.8 (90.8 to 97.4)		

Statistical analyses

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

Number of subjects included in analysis	423
Analysis specification	Pre-specified
Analysis type	non-inferiority[16]
Parameter estimate	Difference in Percentage
Point estimate	5.24
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.83
upper limit	9.85

Notes:

[16] - The two-sided 97.5% CI was calculated based on the Wilson score method without continuity correction. The non-inferiority was demonstrated if the lower limit of the 97.5% CI of the percentage difference between compared groups was >-10%.

Secondary: GMTs of Antibodies Against Meningococcal Serogroup C Measured by rSBA Following Vaccination with MenACYW Conjugate Vaccine or Nimenrix® (Non-inferiority Analysis)

End point title	GMTs of Antibodies Against Meningococcal Serogroup C Measured by rSBA Following Vaccination with MenACYW Conjugate Vaccine or Nimenrix® (Non-inferiority Analysis)[17]

End point description:

GMT titers against Meningococcal Serogroup C were measured by rSBA. Titers were expressed in terms of 1/dilution. Analysis was performed on rSBA PPAS which was a subset that 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 PPAS.

End point type	Secondary

End point timeframe:

Day 30 (post-vaccination)

Notes:

[17] - 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: Data was planned to be collected and analysed for Group 1 and Group 2 only, as pre-specified in protocol.

End point values	Group 1: MenACYW Conjugate Vaccine	Group 2: Nimenrix® Vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	213	210		
Units: titers				
geometric mean (confidence interval 95%)	2143 (1870 to 2456)	315 (252 to 395)		

Statistical analyses

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

Number of subjects included in analysis	423
Analysis specification	Pre-specified
Analysis type	non-inferiority[18]
Parameter estimate	GMT Ratio
Point estimate	6.8
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	5.04
upper limit	9.18

Notes:

[18] - The two-sided 97.5% CI of the ratio of post-vaccination GMTs was calculated using normal approximation of log-transformed titers. The non-inferiority was demonstrated if the lower limit of the two-sided 97.5% CI of the ratio of GMTs between compared groups was >1/1.5.

Secondary: GMTs of Antibodies Against Meningococcal Serogroup C Measured by rSBA Following Vaccination with MenACYW Conjugate Vaccine or Nimenrix® (Superiority Analysis)

End point title	GMTs of Antibodies Against Meningococcal Serogroup C Measured by rSBA Following Vaccination with MenACYW Conjugate Vaccine or Nimenrix® (Superiority Analysis)[19]

End point description:

GMT titers against Meningococcal Serogroup C were measured by rSBA. Titers were expressed in terms of 1/dilution. Analysis was performed on rSBA PPAS which was a subset that 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 PPAS.

End point type	Secondary

End point timeframe:

Day 30 (post-vaccination)

Notes:

[19] - 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: Data was planned to be collected and analysed for Group 1 and Group 2 only, as pre-specified in protocol.

End point values	Group 1: MenACYW Conjugate Vaccine	Group 2: Nimenrix® Vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	213	210		
Units: titers				
geometric mean (confidence interval 95%)	2143 (1870 to 2456)	315 (252 to 395)		

Statistical analyses

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

Number of subjects included in analysis	423
Analysis specification	Pre-specified
Analysis type	superiority[20]
Parameter estimate	GMT Ratio
Point estimate	6.8
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	5.04
upper limit	9.18

Notes:

[20] - The two-sided 97.5% CI of the ratio of post-vaccination GMTs was calculated using normal approximation of log-transformed titers. The superiority was demonstrated if the lower limit of the two-sided 97.5% CI of the ratio of GMTs between compared groups was >1.

Secondary: Percentage of Subjects With Antibody Titers >=1:8 Against Meningococcal Serogroup C Measured by hSBA Following Vaccination with MenACYW Conjugate Vaccine or NeisVac-C® (Non-inferiority Analysis)

End point title	Percentage of Subjects With Antibody Titers >=1:8 Against Meningococcal Serogroup C Measured by hSBA Following Vaccination with MenACYW Conjugate Vaccine or NeisVac-C® (Non-inferiority Analysis)[21]

End point description:

Antibody titers against Meningococcal Serogroup C were measured by hSBA. Analysis was performed on hSBA PPAS which was a subset that 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 PPAS.

End point type	Secondary

End point timeframe:

Day 30 (post-vaccination)

Notes:

[21] - 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: Data was planned to be collected and analysed for Group 1 and Group 3 only, as pre-specified in protocol.

End point values	Group 1: MenACYW Conjugate Vaccine	Group 3: NeisVac-C® Vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	214	216		
Units: percentage of subjects				
number (confidence interval 95%)	99.5 (97.4 to 100)	99.5 (97.4 to 100)		

Statistical analyses

Statistical analysis title	MenACYW Conjugate Vaccine, NeisVac-C®: Serogroup C
Comparison groups	Group 1: MenACYW Conjugate Vaccine v Group 3: NeisVac-C® Vaccine

Number of subjects included in analysis	430
Analysis specification	Pre-specified
Analysis type	non-inferiority[22]
Parameter estimate	Difference in Percentage
Point estimate	0
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	-2.71
upper limit	2.67

Notes:

[22] - The two-sided 97.5% CI was calculated based on the Wilson score method without continuity correction. The non-inferiority was demonstrated if the lower limit of the 97.5% CI of the percentage difference between compared groups was >-10%.

Secondary: GMTs of Antibodies Against Meningococcal Serogroup C Measured by hSBA After Vaccination with MenACYW Conjugate Vaccine or NeisVac-C® (Non-inferiority Analysis)

End point title	GMTs of Antibodies Against Meningococcal Serogroup C Measured by hSBA After Vaccination with MenACYW Conjugate Vaccine or NeisVac-C® (Non-inferiority Analysis)[23]

End point description:

GMT titers against Meningococcal Serogroup C were measured by hSBA. Titers were expressed in terms of 1/dilution. Analysis was performed on hSBA PPAS which was a subset that 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 PPAS.

End point type	Secondary

End point timeframe:

Day 30 (post-vaccination)

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Data was planned to be collected and analysed for Group 1 and Group 3 only, as pre-specified in protocol.

End point values	Group 1: MenACYW Conjugate Vaccine	Group 3: NeisVac-C® Vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	214	216		
Units: titers				
geometric mean (confidence interval 95%)	515 (450 to 591)	227 (198 to 260)		

Statistical analyses

Statistical analysis title	MenACYW Conjugate Vaccine, NeisVac-C®: Serogroup C
Comparison groups	Group 1: MenACYW Conjugate Vaccine v Group 3: NeisVac-C® Vaccine

Number of subjects included in analysis	430
Analysis specification	Pre-specified
Analysis type	non-inferiority[24]
Parameter estimate	GMT Ratio
Point estimate	2.27
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.82
upper limit	2.84

Notes:

[24] - The two-sided 97.5% CI of the ratio of post-vaccination GMTs was calculated using normal approximation of log-transformed titers. The non-inferiority was demonstrated if the lower limit of the two-sided 97.5% CI of the ratio of GMTs between compared groups was >1/1.5.

Secondary: GMTs of Antibodies Against Meningococcal Serogroup C Measured by hSBA Following Vaccination with MenACYW Conjugate Vaccine or NeisVac-C® (Superiority Analysis)

End point title	GMTs of Antibodies Against Meningococcal Serogroup C Measured by hSBA Following Vaccination with MenACYW Conjugate Vaccine or NeisVac-C® (Superiority Analysis)[25]

End point description:

GMT titers against Meningococcal Serogroup C were measured by hSBA. Titers were expressed in terms of 1/dilution. Analysis was performed on hSBA PPAS which was a subset that 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 PPAS.

End point type	Secondary

End point timeframe:

Day 30 (post-vaccination)

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Data was planned to be collected and analysed for Group 1 and Group 3 only, as pre-specified in protocol.

End point values	Group 1: MenACYW Conjugate Vaccine	Group 3: NeisVac-C® Vaccine		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	214	216		
Units: titers				
geometric mean (confidence interval 95%)	515 (450 to 591)	227 (198 to 260)		

Statistical analyses

Statistical analysis title	MenACYW Conjugate Vaccine, NeisVac-C®: Serogroup C
Comparison groups	Group 1: MenACYW Conjugate Vaccine v Group 3: NeisVac-C® Vaccine

Number of subjects included in analysis	430
Analysis specification	Pre-specified
Analysis type	superiority[26]
Parameter estimate	GMT Ratio
Point estimate	2.27
Confidence interval	
level	Other: 97.5 %
sides	2-sided
lower limit	1.82
upper limit	2.84

Notes:

[26] - The two-sided 97.5% CI of the ratio of post-vaccination GMTs was calculated using normal approximation of log-transformed titers. The superiority was demonstrated if the lower limit of the two-sided 97.5% CI of the ratio of GMTs between compared groups was >1.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Unsolicited adverse event (AE) data were collected from Day 0 (pre-vaccination) up to Day 30 (post-vaccination). The solicited reactions (SR) were collected within 7 days post-vaccination. Serious AEs data were collected up to 30 days post-vaccination.

Adverse event reporting additional description:

Analysis was performed on Safety Analysis Set which included all subjects who had received one dose of study vaccine and were analysed according to the vaccine they actually received.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Group 1: MenACYW Conjugate Vaccine

Reporting group description:

Healthy, toddlers aged 12 to 23 months received a single dose of MenACYW Conjugate vaccine on Day 0.

Reporting group title	Group 2: Nimenrix® Vaccine

Reporting group description:

Healthy, toddlers aged 12 to 23 months received a single dose of Nimenrix vaccine on Day 0.

Reporting group title	Group 3: NeisVac-C® Vaccine

Reporting group description:

Healthy, toddlers aged 12 to 23 months received a single dose of NeisVac-C vaccine on Day 0.

Serious adverse events	Group 1: MenACYW Conjugate Vaccine	Group 2: Nimenrix® Vaccine	Group 3: NeisVac-C® Vaccine
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 230 (0.43%)	1 / 232 (0.43%)	2 / 239 (0.84%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Foreign Body In Throat			
subjects affected / exposed	0 / 230 (0.00%)	0 / 232 (0.00%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Febrile Convulsion			
subjects affected / exposed	0 / 230 (0.00%)	1 / 232 (0.43%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			

Urticaria			
subjects affected / exposed	0 / 230 (0.00%)	0 / 232 (0.00%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Respiratory Syncytial Virus Infection			
subjects affected / exposed	1 / 230 (0.43%)	0 / 232 (0.00%)	0 / 239 (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 Tract Infection Viral			
subjects affected / exposed	0 / 230 (0.00%)	0 / 232 (0.00%)	1 / 239 (0.42%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Group 1: MenACYW Conjugate Vaccine	Group 2: Nimenrix® Vaccine	Group 3: NeisVac-C® Vaccine
Total subjects affected by non-serious adverse events			
subjects affected / exposed	197 / 230 (85.65%)	192 / 232 (82.76%)	203 / 239 (84.94%)
Nervous system disorders			
Somnolence			
subjects affected / exposed	40 / 230 (17.39%)	41 / 232 (17.67%)	49 / 239 (20.50%)
occurrences (all)	40	41	49
General disorders and administration site conditions			
Crying			
subjects affected / exposed	72 / 230 (31.30%)	73 / 232 (31.47%)	81 / 239 (33.89%)
occurrences (all)	73	73	82
Injection Site Erythema			
subjects affected / exposed	85 / 230 (36.96%)	95 / 232 (40.95%)	95 / 239 (39.75%)
occurrences (all)	85	95	95
Injection Site Pain			
subjects affected / exposed	96 / 230 (41.74%)	73 / 232 (31.47%)	91 / 239 (38.08%)
occurrences (all)	96	73	91
Injection Site Swelling			

subjects affected / exposed	33 / 230 (14.35%)	34 / 232 (14.66%)	42 / 239 (17.57%)
occurrences (all)	33	34	42
Pyrexia			
subjects affected / exposed	38 / 230 (16.52%)	43 / 232 (18.53%)	45 / 239 (18.83%)
occurrences (all)	41	45	47
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	12 / 230 (5.22%)	14 / 232 (6.03%)	12 / 239 (5.02%)
occurrences (all)	14	18	12
Teething			
subjects affected / exposed	21 / 230 (9.13%)	11 / 232 (4.74%)	14 / 239 (5.86%)
occurrences (all)	22	15	19
Toothache			
subjects affected / exposed	16 / 230 (6.96%)	6 / 232 (2.59%)	7 / 239 (2.93%)
occurrences (all)	20	6	8
Vomiting			
subjects affected / exposed	20 / 230 (8.70%)	20 / 232 (8.62%)	16 / 239 (6.69%)
occurrences (all)	23	20	16
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	11 / 230 (4.78%)	9 / 232 (3.88%)	12 / 239 (5.02%)
occurrences (all)	11	10	13
Psychiatric disorders			
Irritability			
subjects affected / exposed	101 / 230 (43.91%)	101 / 232 (43.53%)	107 / 239 (44.77%)
occurrences (all)	103	101	109
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	22 / 230 (9.57%)	19 / 232 (8.19%)	26 / 239 (10.88%)
occurrences (all)	22	21	26
Rhinitis			
subjects affected / exposed	10 / 230 (4.35%)	8 / 232 (3.45%)	14 / 239 (5.86%)
occurrences (all)	10	8	15
Upper Respiratory Tract Infection			
subjects affected / exposed	15 / 230 (6.52%)	11 / 232 (4.74%)	14 / 239 (5.86%)
occurrences (all)	15	11	14

Metabolism and nutrition disorders Decreased Appetite subjects affected / exposed occurrences (all)	59 / 230 (25.65%) 59	67 / 232 (28.88%) 67	67 / 239 (28.03%) 67

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 May 2020	Following changes were made: number of study centers revised from 20 to 31 centers in European countries; changed end of study period to 4th quarter (Q4) 2020; revised number of study subjects; changed 675 total subjects to 705 total subjects; changed number of subjects in each group from 225 to 235; text modified/added to reflect impact of Coronavirus Disease 2019 (COVID-19) on the planned sample size; to reflect change in sample size from 675 to 705 subjects; text modified/added to reflect impact of COVID-19 on the planned sample size; added new abbreviation for COVID-19; additional section and text for COVID-19 risk assessment per European Union regulatory guidelines; to delineate which tasks would be done by the blinded/unblinded staff; to delineate tasks are for investigator or designate; to reflect changes to clarify blood sample procedures; changed date of final clinical study report to Q2 2021; to add text for amendment 1 justification; concomitant medications updated to reflect COVID-19 changes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
17 March 2020	Due to the COVID-19 pandemic, subject enrollment was put on hold on 17 March 2020.	28 May 2020

Notes:

Limitations and caveats

None reported