Clinical trial results:
Immunogenicity and Safety of an Investigational Quadrivalent Meningococcal Conjugate Vaccine Administered as a Booster Dose in Children Vaccinated 3 Years Earlier as Toddlers

Summary

EudraCT number	2017-001993-40
Trial protocol	FI
Global end of trial date	10 September 2018

Results information

Result version number	v1 (current)
This version publication date	05 January 2020
First version publication date	05 January 2020

Trial information

Trial identification

Sponsor protocol code	MET62

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03476135
WHO universal trial number (UTN)	U1111-1183-5988

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur Inc.
Sponsor organisation address	Discovery Drive, Swiftwater, PA, 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	18 October 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 September 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Immunogenicity:
1) To describe the antibody persistence of meningococcal serogroups A, C, Y, and W before a booster dose in children who received either Meningococcal Polysaccharide (Serogroups A, C, Y, and W) Tetanus Toxoid Conjugate Vaccine (MenACYW) or Nimenrix® 3 years earlier as toddlers.
2) To describe the antibody responses to meningococcal serogroups A, C, Y, and W 30 days after a booster dose of MenACYW conjugate vaccine in children who received either MenACYW conjugate vaccine or Nimenrix® 3 years earlier as toddlers.
3) To describe the antibody responses against tetanus toxoid 30 days after a booster dose of MenACYW conjugate vaccine in children who received either MenACYW conjugate vaccine or Nimenrix® 3 years earlier as toddlers.
Safety:
To describe the safety profile of a booster dose of MenACYW conjugate vaccine in children who received either MenACYW conjugate vaccine or Nimenrix® 3 years earlier as 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 was also available on site in case of any immediate allergic reactions.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 February 2018
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	Finland: 91
Worldwide total number of subjects	91
EEA total number of subjects	91

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)	91
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 at 8 sites in Finland from 27 February 2018 to 7 August 2018.

Pre-assignment

Screening details:

A total of 91 subjects who received a single dose of MenACYW conjugate vaccine or Nimenrix® vaccine in previous study MET54 (EudraCT ID: 2014-004367-20/NCT03205358) were enrolled in this study (MET62).

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

MET62 was an open-label study.

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1:MenACYW Conjugate Vaccine(Previous exposed to MenACYW)

Arm description:

Subjects who received a single dose of MenACYW conjugate vaccine 3 years earlier in a previous vaccine study (MET54), received a booster dose of MenACYW conjugate vaccine at Day 0 in this study (MET62).

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 millilitre (mL), intramuscular, single dose on Day 0.

Arm title	Group2:MenACYW Conjugate Vaccine(Previous Exposed to Nimenrix)

Arm description:

Subjects who received a single dose of Nimenrix® vaccine 3 years earlier in a previous vaccine study (MET54), received a booster dose of MenACYW conjugate vaccine at Day 0 in this study (MET62).

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.

Number of subjects in period 1	Group 1:MenACYW Conjugate Vaccine(Previous exposed to	Group2:MenACYW Conjugate Vaccine(Previous Exposed to
Started	42	49
Completed	42	49

Baseline characteristics

Reporting groups	
Reporting group title	Group 1:MenACYW Conjugate Vaccine(Previous exposed to MenACYW)
Reporting group description:	
Subjects who received a single dose of MenACYW conjugate vaccine 3 years earlier in a previous vaccine study (MET54), received a booster dose of MenACYW conjugate vaccine at Day 0 in this study (MET62).	
Reporting group title	Group2:MenACYW Conjugate Vaccine(Previous Exposed to Nimenrix)
Reporting group description:	
Subjects who received a single dose of Nimenrix® vaccine 3 years earlier in a previous vaccine study (MET54), received a booster dose of MenACYW conjugate vaccine at Day 0 in this study (MET62).	

Reporting group values	Group 1:MenACYW Conjugate Vaccine(Previous exposed to	Group2:MenACYW Conjugate Vaccine(Previous Exposed to	Total
Number of subjects	42	49	91
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	3.9	3.9	
standard deviation	± 0.35	± 0.33	-
Gender categorical			
Units: Subjects			
Female	16	30	46
Male	26	19	45

End points

End points reporting groups

Reporting group title	Group 1:MenACYW Conjugate Vaccine(Previous exposed to MenACYW)

Reporting group description:

Subjects who received a single dose of MenACYW conjugate vaccine 3 years earlier in a previous vaccine study (MET54), received a booster dose of MenACYW conjugate vaccine at Day 0 in this study (MET62).

Reporting group title	Group2:MenACYW Conjugate Vaccine(Previous Exposed to Nimenrix)

Reporting group description:

Subjects who received a single dose of Nimenrix® vaccine 3 years earlier in a previous vaccine study (MET54), received a booster dose of MenACYW conjugate vaccine at Day 0 in this study (MET62).

Primary: Antibody Titers (hSBA) Against Meningococcal Serogroups A, C, Y, and W Before a Booster Dose of MenACYW Conjugate Vaccine

End point title	Antibody Titers (hSBA) Against Meningococcal Serogroups A, C, Y, and W Before a Booster Dose of MenACYW Conjugate Vaccine[1]

End point description:

Antibody titers against meningococcal serogroups A, C, Y, and W were measured by serum bactericidal assay using human complement (hSBA). Analysis was performed on Per-Protocol Analysis Set (PPAS) which included all subjects who received at least 1 dose of the study vaccine, had a valid post-vaccination blood sample results and had no protocol deviations.

End point type	Primary

End point timeframe:

Day 0

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint was descriptive in nature, no statistical analysis was provided.

End point values	Group 1:MenACYW Conjugate Vaccine(Previous exposed to MenACYW)	Group2:MenACYW Conjugate Vaccine(Previous Exposed to Nimenrix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	44		
Units: titers (1/dilution)				
geometric mean (confidence interval 95%)				
Serogroup A	12.1 (8.15 to 18.1)	16.5 (11.9 to 22.9)		
Serogroup C	106 (73.2 to 153)	11.7 (7.03 to 19.4)		
Serogroup Y	30.9 (24.2 to 39.5)	17.6 (13.1 to 23.7)		
Serogroup W	48.5 (34.4 to 68.4)	21.9 (14.7 to 32.7)		

Statistical analyses

No statistical analyses for this end point

Primary: Antibody Titers (hSBA) Against Meningococcal Serogroups A, C, Y, and W After a Booster Dose of MenACYW Conjugate Vaccine

End point title	Antibody Titers (hSBA) Against Meningococcal Serogroups A, C, Y, and W After a Booster Dose of MenACYW Conjugate Vaccine[2]

End point description:

Antibody titers against meningococcal serogroups A, C, Y, and W were measured by hSBA. Analysis was performed on PPAS.

End point type	Primary

End point timeframe:

Day 30 (post-booster vaccination)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint was descriptive in nature, no statistical analysis was provided.

End point values	Group 1:MenACYW Conjugate Vaccine(Previous exposed to MenACYW)	Group2:MenACYW Conjugate Vaccine(Previous Exposed to Nimenrix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	44		
Units: titers (1/dilution)				
geometric mean (confidence interval 95%)				
Serogroup A	763 (521 to 1117)	659 (427 to 1017)		
Serogroup C	5894 (4325 to 8031)	1592 (1165 to 2174)		
Serogroup Y	2013 (1451 to 2792)	2806 (2066 to 3813)		
Serogroup W	2656 (1601 to 4406)	3444 (2387 to 4970)		

Statistical analyses

No statistical analyses for this end point

Primary: Antibody Titers (rSBA) Against Meningococcal Serogroups A, C, Y, and W Before a Booster Dose of MenACYW Conjugate Vaccine

End point title	Antibody Titers (rSBA) Against Meningococcal Serogroups A, C,

	Y, and W Before a Booster Dose of MenACYW Conjugate Vaccine[3]

End point description:

Antibody titers against meningococcal serogroups A, C, Y, and W were measured by serum bactericidal assay using baby rabbit complement (rSBA). Analysis was performed on PPAS. Here, 'number of subjects analysed' = subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Day 0

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint was descriptive in nature, no statistical analysis was provided.

End point values	Group 1:MenACYW Conjugate Vaccine(Previous exposed to MenACYW)	Group2:MenACYW Conjugate Vaccine(Previous Exposed to Nimenrix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	44		
Units: titers (1/dilution)				
geometric mean (confidence interval 95%)				
Serogroup A	135 (58.0 to 314)	281 (131 to 606)		
Serogroup C	102 (60.9 to 169)	11.9 (6.14 to 22.9)		
Serogroup Y	119 (65.0 to 219)	126 (69.1 to 230)		
Serogroup W	113 (54.6 to 234)	126 (63.6 to 250)		

Statistical analyses

No statistical analyses for this end point

Primary: Antibody Titers (rSBA) Against Meningococcal Serogroups A, C, Y, and W After a Booster Dose of MenACYW Conjugate Vaccine

End point title	Antibody Titers (rSBA) Against Meningococcal Serogroups A, C, Y, and W After a Booster Dose of MenACYW Conjugate Vaccine[4]

End point description:

Antibody titers against meningococcal serogroups A, C, Y, and W were measured by rSBA. Analysis was performed on PPAS.

End point type	Primary

End point timeframe:

Day 30 (post-booster vaccination)

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint was descriptive in nature, no statistical analysis was provided.

End point values	Group 1:MenACYW Conjugate Vaccine(Previous exposed to MenACYW)	Group2:MenACYW Conjugate Vaccine(Previous Exposed to Nimenrix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	44		
Units: titers (1/dilution)				
geometric mean (confidence interval 95%)				
Serogroup A	4240 (3352 to 5365)	5702 (4575 to 7107)		
Serogroup C	8629 (6573 to 11328)	4871 (3750 to 6327)		
Serogroup Y	5499 (4502 to 6717)	7814 (6465 to 9445)		
Serogroup W	16103 (12691 to 20431)	19793 (15538 to 25214)		

Statistical analyses

No statistical analyses for this end point

Primary: Antibody Titers (hSBA) Against Meningococcal Serogroups A, C, Y, and W for Priming Vaccination in MET54 and Booster Vaccination in MET62

End point title	Antibody Titers (hSBA) Against Meningococcal Serogroups A, C, Y, and W for Priming Vaccination in MET54 and Booster Vaccination in MET62[5]

End point description:

Antibody titers against meningococcal serogroups A, C, Y, and W were measured by hSBA. Analysis was performed on Full Analysis Set for Persistence (FASP) which included all subjects who had a valid pre-vaccination blood sample result. Here 'n' signifies number of subjects with available data for specified category and "-99999" & "99999" signifies no data calculated for 95% confidence interval field, because everyone’s baseline value in MET54 was 2 for the specified category.

End point type	Primary

End point timeframe:

Day 0 from study MET54, Day 30 (post-priming vaccination) from study MET54, Day 0 from study MET62 and Day 30 (post booster-vaccination) from study MET62

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint was descriptive in nature, no statistical analysis was provided.

End point values	Group 1:MenACYW Conjugate Vaccine(Previous exposed to MenACYW)	Group2:MenACYW Conjugate Vaccine(Previous Exposed to Nimenrix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	49		
Units: titers (1/dilution)				
geometric mean (confidence interval 95%)				

Serogroup A: Day 0 (MET54) (n=41,49)	3.68 (3.12 to 4.33)	3.67 (3.15 to 4.29)		
Serogroup A: Day 30 (MET54) (n=42,49)	83.3 (63.9 to 109)	49.6 (32.1 to 76.7)		
Serogroup A: Day 0 (MET62) (n=42,49)	11.9 (8.11 to 17.4)	14.7 (10.7 to 20.2)		
Serogroup A: Day 30 (MET62) (n=41,47)	755 (520 to 1097)	629 (418 to 948)		
Serogroup C: Day 0 (MET54) (n=42,49)	2.48 (2.04 to 3.01)	2.30 (2.12 to 2.50)		
Serogroup C: Day 30 (MET54) (n=42,49)	594 (445 to 793)	29.4 (20.1 to 43.1)		
Serogroup C: Day 0 (MET62) (n=42,49)	103 (71.7 to 149)	11.6 (7.28 to 18.3)		
Serogroup C: Day 30 (MET62) (n=41,47)	5744 (4230 to 7800)	1618 (1204 to 2172)		
Serogroup Y: Day 0 (MET54) (n=42,49)	2.17 (1.95 to 2.42)	2.27 (2.05 to 2.52)		
Serogroup Y: Day 30 (MET54) (n=42,49)	105 (73.9 to 149)	75.8 (54.2 to 106)		
Serogroup Y: Day 0 (MET62) (n=42,49)	32.5 (24.8 to 42.7)	18.2 (13.8 to 24.0)		
Serogroup Y: Day 30 (MET62) (n=41,47)	2048 (1486 to 2823)	2710 (2022 to 3633)		
Serogroup W: Day 0 (MET54) (n=42,49)	2.00 (-99999 to 99999)	2.12 (2.00 to 2.24)		
Serogroup W: Day 30 (MET54) (n=42,49)	71.8 (53.3 to 96.7)	40.1 (30.6 to 52.6)		
Serogroup W: Day 0 (MET62) (n=42,49)	50.0 (35.9 to 69.5)	21.2 (14.6 to 30.9)		
Serogroup W: Day 30 (MET62) (n=41,47)	2776 (1682 to 4584)	3235 (2278 to 4594)		

Statistical analyses

No statistical analyses for this end point

Primary: Antibody Titers (rSBA) Against Meningococcal Serogroups A, C, Y, and W for Priming Vaccination in MET54 and Booster Vaccination in MET62

End point title	Antibody Titers (rSBA) Against Meningococcal Serogroups A, C, Y, and W for Priming Vaccination in MET54 and Booster Vaccination in MET62[6]

End point description:

Antibody titers against meningococcal serogroups A, C, Y, and W were measured by rSBA. Analysis was performed on FASP. Here 'n' signifies number of subjects with available data for specified category and "-99999" &"99999" signifies no data calculated for 95% confidence interval field, because everyone’s baseline value in MET54 was 2 for the specified category.

End point type	Primary

End point timeframe:

Day 0 from study MET54, Day 30 (post-priming vaccination) from study MET54, Day 0 from study MET62 and Day 30 (post booster-vaccination) from study MET62

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint was descriptive in nature, no statistical analysis was provided.

End point values	Group 1:MenACYW Conjugate Vaccine(Previous exposed to MenACYW)	Group2:MenACYW Conjugate Vaccine(Previous Exposed to Nimenrix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	49		
Units: titers (1/dilution)				
geometric mean (confidence interval 95%)				
Serogroup A: Day 0 (MET54) (n=42,49)	12.3 (5.25 to 28.8)	4.88 (2.74 to 8.69)		
Serogroup A: Day 30 (MET54) (n=42,49)	3198 (2559 to 3996)	7633 (5879 to 9909)		
Serogroup A: Day 0 (MET62) (n=41,49)	124 (54.0 to 283)	239 (113 to 503)		
Serogroup A: Day 30 (MET62) (n=41,47)	4096 (3223 to 5205)	5341 (4275 to 6674)		
Serogroup C: Day 0 (MET54) (n=42,49)	2.21 (1.81 to 2.70)	2.15 (1.86 to 2.47)		
Serogroup C: Day 30 (MET54) (n=42,49)	2711 (2156 to 3409)	414 (283 to 607)		
Serogroup C: Day 0 (MET62) (n=41,49)	94.4 (55.9 to 160)	11.2 (6.11 to 20.6)		
Serogroup C: Day 30 (MET62) (n=41,47)	8474 (6483 to 11075)	4817 (3759 to 6175)		
Serogroup Y: Day 0 (MET54) (n=42,49)	2.88 (1.87 to 4.42)	4.29 (2.48 to 7.44)		
Serogroup Y: Day 30 (MET54) (n=42,49)	2667 (2063 to 3447)	2836 (2127 to 3781)		
Serogroup Y: Day 0 (MET62) (n=41,49)	120 (67.1 to 213)	123 (67.6 to 223)		
Serogroup Y: Day 30 (MET62) (n=41,47)	5553 (4565 to 6755)	7498 (6213 to 9049)		
Serogroup W: Day 0 (MET54) (n=42,49)	2.00 (-99999 to 99999)	2.24 (1.78 to 2.81)		
Serogroup W: Day 30 (MET54) (n=42,49)	5793 (4346 to 7720)	4214 (3162 to 5616)		
Serogroup W: Day 0 (MET62) (n=41,49)	106 (51.6 to 219)	113 (57.9 to 219)		
Serogroup W: Day 30 (MET62) (n=41,47)	15839 (12530 to 20023)	18710 (14737 to 23753)		

Statistical analyses

No statistical analyses for this end point

Primary: Antibody Concentrations Against Tetanus Toxoid Before a Booster Dose of MenACYW Conjugate Vaccine

End point title	Antibody Concentrations Against Tetanus Toxoid Before a Booster Dose of MenACYW Conjugate Vaccine[7]

End point description:

Anti-tetanus antibodies were measured by electrochemiluminescent (ECL) assay. Analysis was performed on PPAS. Here, 'number of subjects analysed' = subjects evaluable for this endpoint.

End point type	Primary

End point timeframe:

Day 0

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint was descriptive in nature, no statistical analysis was provided.

End point values	Group 1:MenACYW Conjugate Vaccine(Previous exposed to MenACYW)	Group2:MenACYW Conjugate Vaccine(Previous Exposed to Nimenrix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	44		
Units: International Unit per millilitre(IU/mL)				
geometric mean (confidence interval 95%)	3.12 (2.05 to 4.75)	3.02 (2.11 to 4.31)		

Statistical analyses

No statistical analyses for this end point

Primary: Antibody Concentrations Against Tetanus Toxoid After a Booster Dose of MenACYW Conjugate Vaccine

End point title	Antibody Concentrations Against Tetanus Toxoid After a Booster Dose of MenACYW Conjugate Vaccine[8]

End point description:

Anti-tetanus antibodies were measured by ECL assay. Analysis was performed on PPAS.

End point type	Primary

End point timeframe:

Day 30 (post-booster vaccination)

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint was descriptive in nature, no statistical analysis was provided.

End point values	Group 1:MenACYW Conjugate Vaccine(Previous exposed to MenACYW)	Group2:MenACYW Conjugate Vaccine(Previous Exposed to Nimenrix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	44		
Units: IU/mL				
geometric mean (confidence interval 95%)	10.4 (8.41 to 12.8)	9.36 (7.61 to 11.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Immediate Adverse Event After Vaccination

End point title	Number of Subjects With Immediate Adverse Event After Vaccination[9]

End point description:

Immediate events captured medically relevant unsolicited systemic adverse events (AEs) that occurred within the first 30 minutes after vaccination. An unsolicited AE was an observed AE that did not fulfill the conditions prelisted in the case report book (CRB) in terms of diagnosis and/or onset window post-vaccination. Systemic AEs were all AEs that were not injection or administration site reactions. Analysis was performed on safety analysis set which included subjects who had received at least one dose of the study vaccine and had any safety data available.

End point type	Primary

End point timeframe:

Within 30 minutes after vaccination

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint was descriptive in nature, no statistical analysis was provided.

End point values	Group 1:MenACYW Conjugate Vaccine(Previous exposed to MenACYW)	Group2:MenACYW Conjugate Vaccine(Previous Exposed to Nimenrix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	49		
Units: subjects				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Solicited Injection Site Reactions and Systemic Reactions

End point title	Number of Subjects With Solicited Injection Site Reactions and Systemic Reactions[10]

End point description:

A solicited reaction (SR) was an adverse reaction (AR) observed and reported under the conditions (nature and onset) prelisted in the protocol and CRB. Solicited injection site reactions: pain, erythema, and swelling. Solicited systemic reactions: fever, headache, malaise and, myalgia. Analysis was performed on safety analysis set.

End point type	Primary

End point timeframe:

Within 7 days after vaccination

Notes:

[10] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint was descriptive in nature, no statistical analysis was provided.

End point values	Group 1:MenACYW Conjugate Vaccine(Previous exposed to MenACYW)	Group2:MenACYW Conjugate Vaccine(Previous Exposed to Nimenrix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	49		
Units: subjects				
number (not applicable)				
Pain	26	35		
Erythema	22	27		
Swelling	16	19		
Fever	3	4		
Headache	8	14		
Malaise	13	15		
Myalgia	14	21		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Unsolicited Adverse Event After Vaccination

End point title	Number of Subjects with Unsolicited Adverse Event After Vaccination[11]

End point description:

An unsolicited AE was an observed AE that did not fulfill the conditions prelisted in the CRB in terms of diagnosis and/or onset window post-vaccination. Analysis was performed on safety analysis set.

End point type	Primary

End point timeframe:

Within 30 days after vaccination

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint was descriptive in nature, no statistical analysis was provided.

End point values	Group 1:MenACYW Conjugate Vaccine(Previous exposed to MenACYW)	Group2:MenACYW Conjugate Vaccine(Previous Exposed to Nimenrix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	49		
Units: subjects				
number (not applicable)	22	15		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with a Serious Adverse Event (SAE) During the Study

End point title	Number of Subjects with a Serious Adverse Event (SAE) During the Study[12]

End point description:

A SAE is any untoward medical occurrence that at any dose results in death, is life-threatening, requires inpatient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, is an important medical event. Analysis was performed on safety analysis set.

End point type	Primary

End point timeframe:

Within 30 days after vaccination

Notes:

[12] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint was descriptive in nature, no statistical analysis was provided.

End point values	Group 1:MenACYW Conjugate Vaccine(Previous exposed to MenACYW)	Group2:MenACYW Conjugate Vaccine(Previous Exposed to Nimenrix)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	49		
Units: subjects				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SR were collected up to Day 7 after each vaccination, non-serious unsolicited AEs were collected up to Day 30 after each vaccination. SAEs were collected throughout the trial (up to 30 days after vaccination).

Adverse event reporting additional description:

SR was an AR observed and reported under the conditions (nature and onset) prelisted in the protocol and CRB. An unsolicited AE was an observed AE that did not fulfill the conditions prelisted in the CRB in terms of diagnosis and/or onset window post-vaccination. Analysis was performed on safety analysis set.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Group 1:MenACYW Conjugate Vaccine(Previous exposed to MenACYW)

Reporting group description:

Subjects who received a single dose of MenACYW conjugate vaccine 3 years earlier in a previous vaccine study (MET54), received a booster dose of MenACYW conjugate vaccine at Day 0 in this study (MET62).

Reporting group title	Group2:MenACYW Conjugate Vaccine(Previous Exposed to Nimenrix)

Reporting group description:

Subjects who received a single dose of Nimenrix® vaccine 3 years earlier in a previous vaccine study (MET54), received a booster dose of MenACYW conjugate vaccine at Day 0 in this study (MET62).

Serious adverse events	Group 1:MenACYW Conjugate Vaccine(Previous exposed to	Group2:MenACYW Conjugate Vaccine(Previous Exposed to	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 42 (0.00%)	0 / 49 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Group 1:MenACYW Conjugate Vaccine(Previous exposed to	Group2:MenACYW Conjugate Vaccine(Previous Exposed to	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 42 (85.71%)	43 / 49 (87.76%)	
Nervous system disorders			

Headache			
subjects affected / exposed	10 / 42 (23.81%)	14 / 49 (28.57%)	
occurrences (all)	11	14	
General disorders and administration site conditions			
Injection Site Erythema			
subjects affected / exposed	22 / 42 (52.38%)	27 / 49 (55.10%)	
occurrences (all)	22	27	
Injection Site Pain			
subjects affected / exposed	26 / 42 (61.90%)	35 / 49 (71.43%)	
occurrences (all)	26	35	
Injection Site Swelling			
subjects affected / exposed	16 / 42 (38.10%)	19 / 49 (38.78%)	
occurrences (all)	16	19	
Malaise			
subjects affected / exposed	13 / 42 (30.95%)	15 / 49 (30.61%)	
occurrences (all)	13	15	
Pyrexia			
subjects affected / exposed	3 / 42 (7.14%)	4 / 49 (8.16%)	
occurrences (all)	3	4	
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	14 / 42 (33.33%)	21 / 49 (42.86%)	
occurrences (all)	14	21	
Infections and infestations			
Otitis Media			
subjects affected / exposed	1 / 42 (2.38%)	3 / 49 (6.12%)	
occurrences (all)	1	3	
Upper Respiratory Tract Infection			
subjects affected / exposed	7 / 42 (16.67%)	4 / 49 (8.16%)	
occurrences (all)	7	4	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 March 2018	Following changes were made: Updated department name for the Pharmacovigilance Global Safety Expert; updated the planned trial period and planned trial calendar information; updated description of the need for a physical examination or assessment of health in the case of a rescheduled Visit 1; clarified concomitant medications and other therapies; updated the assay method used to measure anti-tetanus antibodies; addition of references to the Adverse event of special interest (AESI) of generalised seizures and to the AESI of Kawasaki disease.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported