Clinical trial results:
A Phase II Study of the Immunogenicity and Safety of an Investigational Quadrivalent Meningococcal Conjugate Vaccine in Healthy Toddlers

Summary

EudraCT number	2014-004367-20
Trial protocol	FI
Global end of trial date	19 August 2015

Results information

Result version number	v1 (current)
This version publication date	09 June 2016
First version publication date	09 June 2016

Trial information

Trial identification

Sponsor protocol code	MET54

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	U1111-1143-8912

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur Inc.
Sponsor organisation address	1 Discovery Drive, Swiftwater, United States, 18370
Public contact	Responsible Medical Officer, Clinical Development, Sanofi Pasteur Inc., +1 570-957-3570, emilia.jordanov@sanofipasteur.com
Scientific contact	Responsible Medical Officer, Clinical Development, Sanofi Pasteur Inc., +1 570-957-3570, emilia.jordanov@sanofipasteur.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?	No

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	11 April 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 August 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Observational objectives:
- To evaluate the antibody responses to the antigens (serogroups A, C, Y, and W) present in MenACYW conjugate vaccine and NIMENRIX® measured by serum bactericidal assay using baby rabbit complement (rSBA) and by serum bactericidal assay using human complement (hSBA)
- To evaluate the antibody responses against tetanus in subjects who received MenACYW conjugate vaccine or NIMENRIX vaccine
- To evaluate the safety profile of MenACYW conjugate vaccine and NIMENRIX®

Protection of trial subjects:

Only subjects that met all the study inclusion and none of the exclusion criteria were randomized and vaccinated in the study. 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:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	31 March 2015
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: 188
Worldwide total number of subjects	188
EEA total number of subjects	188

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	188

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 from 31 March 2015 to 17 July 2015 at 8 clinic centers in Finland.

Pre-assignment

Screening details:

A total of 188 subjects who met all inclusion and none of the 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	Not blinded

Blinding implementation details:

Not applicable

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1: MenACYW conjugate vaccine

Arm description:

Healthy, meningococcal-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: NIMENRIX®

Arm description:

Healthy, meningococcal-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

Number of subjects in period 1	Group 1: MenACYW conjugate vaccine	Group 2: NIMENRIX®
Started	94	94
Completed	94	94

Baseline characteristics

Reporting groups	
Reporting group title	Group 1: MenACYW conjugate vaccine
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®
Reporting group description:	
Healthy, meningococcal-vaccine naive toddlers aged 12 to 23 months received a single dose of NIMENRIX® vaccine.	

Reporting group values	Group 1: MenACYW conjugate vaccine	Group 2: NIMENRIX®	Total
Number of subjects	94	94	188
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	94	94	188
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	1.44	1.47	
standard deviation	± 0.302	± 0.314	-
Gender categorical Units: Subjects			
Female	37	53	90
Male	57	41	98

End points

End points reporting groups

Reporting group title	Group 1: MenACYW conjugate vaccine
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®
Reporting group description:	
Healthy, meningococcal-vaccine naive toddlers aged 12 to 23 months received a single dose of NIMENRIX® vaccine.	

Primary: Percentage of Subjects Reporting Solicited Injection-Site or Systemic Reaction Following Vaccination with Either MenACYW Conjugate Vaccine or NIMENRIX®

End point title	Percentage of Subjects Reporting Solicited Injection-Site or Systemic Reaction Following Vaccination with Either MenACYW Conjugate Vaccine or NIMENRIX®[1]

End point description:

Solicited injection site reactions: Tenderness, Erythema, and Swelling. Solicited systemic reactions: Fever, Vomiting, Crying abnormal, Drowsiness, Appetite lost, and Irritability.

Grade 3 solicited injection site reactions: Tenderness, Cries when injected limb is moved or the movement of the injected limb is reduced; Erythema and Swelling, ≥ 50 mm. Grade 3 systemic reactions: Fever, > 39.5°C; Vomiting, ≥ 6 episodes per 24 hours or requiring parenteral hydration; Crying abnormal, > 3 hours; Drowsiness, Sleeping most of the time or difficult to wake up; Appetite lost, Refuses ≥ 3 feeds or refuses most feeds; Irritability, Inconsolable.

End point type	Primary

End point timeframe:

Day 0 up to Day 7 post-vaccination

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: Descriptive analyses were performed based on the study groups and the study vaccine administered for this outcome.

End point values	Group 1: MenACYW conjugate vaccine	Group 2: NIMENRIX®		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	94	94		
Units: Percentage of subjects				
number (not applicable)				
Any Injection site Tenderness	29.8	33		
Grade 3 Any Injection site Tenderness	0	1.1		
Any Injection site Erythema	30.9	35.1		
Grade 3 Injection site Erythema	2.1	1.1		
Any Injection site Swelling	14.9	18.1		
Grade 3 Injection site Swelling	1.1	3.2		
Any Fever	7.4	4.4		
Grade 3 Fever	1.1	0		
Any Vomiting	4.3	5.3		
Grade 3 Vomiting	0	0		

Any Abnormal Crying	33	39.4		
Grade 3 Abnormal Crying	1.1	0		
Any Drowsiness	34	27.7		
Grade 3 Drowsiness	0	0		
Any Loss of appetite	23.4	36.2		
Grade 3 Loss of appetite	1.1	1.1		
Any Irritability	52.1	56.4		
Grade 3 Irritability	0	2.1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Adverse event data were collected from Day 0 up to Day 30 post-vaccination.	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.0
Reporting groups	
Reporting group title	Group 1: MenACYW conjugate vaccine
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®
Reporting group description:	
Healthy, meningococcal-vaccine naive toddlers aged 12 to 23 months received a single dose of NIMENRIX® vaccine.	

Serious adverse events	Group 1: MenACYW conjugate vaccine	Group 2: NIMENRIX®	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 94 (1.06%)	0 / 94 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Ligament injury			
subjects affected / exposed	1 / 94 (1.06%)	0 / 94 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	1 / 94 (1.06%)	0 / 94 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	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®	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	49 / 94 (52.13%)	53 / 94 (56.38%)	
Nervous system disorders			
Drowsiness			
alternative assessment type: Systematic			
subjects affected / exposed	32 / 94 (34.04%)	26 / 94 (27.66%)	
occurrences (all)	32	26	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 94 (2.13%)	6 / 94 (6.38%)	
occurrences (all)	2	7	
Injection site Tenderness			
alternative assessment type: Systematic			
subjects affected / exposed	28 / 94 (29.79%)	31 / 94 (32.98%)	
occurrences (all)	28	31	
Injection site Erythema			
alternative assessment type: Systematic			
subjects affected / exposed	29 / 94 (30.85%)	33 / 94 (35.11%)	
occurrences (all)	29	33	
Injection site Swelling			
alternative assessment type: Systematic			
subjects affected / exposed	14 / 94 (14.89%)	17 / 94 (18.09%)	
occurrences (all)	14	17	
Fever			
alternative assessment type: Systematic			
subjects affected / exposed	7 / 94 (7.45%)	4 / 94 (4.26%)	
occurrences (all)	7	4	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	8 / 94 (8.51%)	4 / 94 (4.26%)	
occurrences (all)	8	4	
Vomiting			
alternative assessment type: Systematic			

subjects affected / exposed	4 / 94 (4.26%)	5 / 94 (5.32%)	
occurrences (all)	4	5	
Psychiatric disorders			
Abnormal crying			
alternative assessment type: Systematic			
subjects affected / exposed	31 / 94 (32.98%)	37 / 94 (39.36%)	
occurrences (all)	31	37	
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed	49 / 94 (52.13%)	53 / 94 (56.38%)	
occurrences (all)	49	53	
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	2 / 94 (2.13%)	7 / 94 (7.45%)	
occurrences (all)	2	7	
Nasopharyngitis			
subjects affected / exposed	9 / 94 (9.57%)	5 / 94 (5.32%)	
occurrences (all)	9	5	
Otitis media			
subjects affected / exposed	4 / 94 (4.26%)	6 / 94 (6.38%)	
occurrences (all)	4	6	
Respiratory tract infection			
subjects affected / exposed	5 / 94 (5.32%)	1 / 94 (1.06%)	
occurrences (all)	7	1	
Rhinitis			
subjects affected / exposed	7 / 94 (7.45%)	5 / 94 (5.32%)	
occurrences (all)	7	5	
Upper respiratory tract infection			
subjects affected / exposed	8 / 94 (8.51%)	16 / 94 (17.02%)	
occurrences (all)	8	16	
Metabolism and nutrition disorders			
Loss of appetite			
alternative assessment type: Systematic			
subjects affected / exposed	22 / 94 (23.40%)	34 / 94 (36.17%)	
occurrences (all)	22	34	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 July 2015	Updated the coordinating investigator, provided trial center information, updated the planned trial period and planned trial calendar information, updated the Control Product information, clarified the vaccine injection sites and labeling and packaging for the investigational and control vaccines, and also updated the description of the rSBA method.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported