# 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<br>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<br>Units: years | | | |
| arithmetic mean | 1.44 | 1.47 | |
| standard deviation | ± 0.302 | ± 0.314 | - |
| Gender categorical<br>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