



## Clinical trial results:

**A phase 3, multi-center, observer-blind, placebo-controlled, randomized study to evaluate the immunogenicity and safety of Novartis Meningococcal ACWY conjugate vaccine in healthy subjects from 11 to 55 years of age in Korea.**

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

## Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2014-005055-11 |
| Trial protocol           | Outside EU/EEA |
| Global end of trial date | 16 March 2011  |

## Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v2 (current)  |
| This version publication date  | 10 June 2016  |
| First version publication date | 02 April 2015 |
| Version creation reason        |               |

## Trial information

### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | V59_39 |
|-----------------------|--------|

### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01274897 |
| WHO universal trial number (UTN)   | -           |

Notes:

## Sponsors

|                              |                                                                                                      |
|------------------------------|------------------------------------------------------------------------------------------------------|
| Sponsor organisation name    | Novartis Vaccines and Diagnostics S.r.l                                                              |
| Sponsor organisation address | Via Fiorentina, 1, Siena, Italy, 53100                                                               |
| Public contact               | Posting director, Novartis Vaccines and Diagnostics S.r.l,<br>RegistryContactVaccinesUS@novartis.com |
| Scientific contact           | Posting director, Novartis Vaccines and Diagnostics S.r.l,<br>RegistryContactVaccinesUS@novartis.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 October 2011 |
| Is this the analysis of the primary completion data? | Yes             |
| Primary completion date                              | 16 March 2011   |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 16 March 2011   |
| Was the trial ended prematurely?                     | No              |

Notes:

## General information about the trial

Main objective of the trial:

Primary Immunogenicity objectives :

To assess the immunogenicity of a single injection of MenACWY as measured by the percentage of subjects with hSBA seroresponse, directed against N meningitidis serogroups A, C, W and Y.

Protection of trial subjects:

This trial was performed with the ethical principles that have their origin in the Declaration of Helsinki, that are consistent with Good Clinical Practice (GCP) according to International Conference on Harmonisation (ICH) guidelines, the applicable regulatory requirements(s) for the country in which the study was conducted, and applicable standard operating procedures (SOPs).

Background therapy: -

Evidence for comparator:

Placebo - One 0.5mL of saline placebo was administered by intramuscular (IM) injection in the deltoid area of the nondominant arm.

|                                                           |                  |
|-----------------------------------------------------------|------------------|
| Actual start date of recruitment                          | 20 December 2010 |
| 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 | Korea, Democratic People's Republic of: 450 |
| Worldwide total number of subjects   | 450                                         |
| EEA total number of subjects         | 0                                           |

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)                     | 37  |
| Adolescents (12-17 years)                 | 230 |
| Adults (18-64 years)                      | 183 |
| From 65 to 84 years                       | 0   |

|                   |   |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

## Subject disposition

### Recruitment

Recruitment details:

Subjects were enrolled from 8 centres in Korea.

### Pre-assignment

Screening details:

All enrolled subjects were included in the trial.

### 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                | Investigator, Subject          |

### Arms

|                              |             |
|------------------------------|-------------|
| Are arms mutually exclusive? | Yes         |
| <b>Arm title</b>             | MenACWY-CRM |

Arm description:

Subjects received one dose of MenACWY-CRM conjugate vaccine.

|                                        |                                                                                             |
|----------------------------------------|---------------------------------------------------------------------------------------------|
| Arm type                               | Experimental                                                                                |
| Investigational medicinal product name | Meningococcal (groups A, C, W, and Y) oligosaccharide diphtheria CRM-197 conjugate vaccine. |
| Investigational medicinal product code |                                                                                             |
| Other name                             |                                                                                             |
| Pharmaceutical forms                   | Powder and solution for solution for injection                                              |
| Routes of administration               | Intramuscular use                                                                           |

Dosage and administration details:

One 0.5mL dose of MenACWY was administered by intramuscular (IM) injection in the deltoid area of nondominant arm.

|                  |         |
|------------------|---------|
| <b>Arm title</b> | Placebo |
|------------------|---------|

Arm description:

Subjects received the saline placebo.

|                                        |                        |
|----------------------------------------|------------------------|
| Arm type                               | Placebo                |
| Investigational medicinal product name | Saline Placebo         |
| Investigational medicinal product code |                        |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Intramuscular use      |

Dosage and administration details:

One 0.5mL of saline placebo was administered by intramuscular (IM) injection in the deltoid area of the nondominant arm.

| <b>Number of subjects in period 1</b> | MenACWY-CRM | Placebo |
|---------------------------------------|-------------|---------|
| Started                               | 297         | 153     |
| Completed                             | 297         | 153     |

## Baseline characteristics

### Reporting groups

|                       |             |
|-----------------------|-------------|
| Reporting group title | MenACWY-CRM |
|-----------------------|-------------|

Reporting group description:

Subjects received one dose of MenACWY-CRM conjugate vaccine.

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Subjects received the saline placebo.

| Reporting group values                                                  | MenACWY-CRM   | Placebo       | Total |
|-------------------------------------------------------------------------|---------------|---------------|-------|
| Number of subjects                                                      | 297           | 153           | 450   |
| Age categorical<br>Units: Subjects                                      |               |               |       |
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | 19.6<br>± 9.2 | 19.3<br>± 8.9 | -     |
| Gender categorical<br>Units: Subjects                                   |               |               |       |
| Female                                                                  | 139           | 77            | 216   |
| Male                                                                    | 158           | 76            | 234   |

## End points

### End points reporting groups

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |                                               |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------|
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | MenACWY-CRM                                   |
| Reporting group description:<br>Subjects received one dose of MenACWY-CRM conjugate vaccine.                                                                                                                                                                                                                                                                                                                                                                                                  |                                               |
| Reporting group title                                                                                                                                                                                                                                                                                                                                                                                                                                                                         | Placebo                                       |
| Reporting group description:<br>Subjects received the saline placebo.                                                                                                                                                                                                                                                                                                                                                                                                                         |                                               |
| Subject analysis set title                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Modified Intention-to-treat (MITT) population |
| Subject analysis set type                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Modified intention-to-treat                   |
| Subject analysis set description:<br>All randomized subjects who received the vaccine, and provided at least one evaluable serum sample before and one after vaccination.                                                                                                                                                                                                                                                                                                                     |                                               |
| Subject analysis set title                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Per protocol population - Immunogenicity      |
| Subject analysis set type                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Per protocol                                  |
| Subject analysis set description:<br>All subjects in the MITT Set who received all the relevant doses of vaccine correctly, and provided evaluable serum samples at the relevant timepoints, and had no major protocol violation as defined prior to unblinding. A "major" deviation is defined as a protocol deviation that is considered to have a significant impact on the immunogenicity results of the subject compared to the result that would have possibly otherwise been obtained. |                                               |
| Subject analysis set title                                                                                                                                                                                                                                                                                                                                                                                                                                                                    | Safety population                             |
| Subject analysis set type                                                                                                                                                                                                                                                                                                                                                                                                                                                                     | Safety analysis                               |
| Subject analysis set description:<br>All subjects who were injected and who had post-injection safety data.                                                                                                                                                                                                                                                                                                                                                                                   |                                               |

### **Primary: To assess the immunogenicity of a single injection of MenACWY as measured by the percentage of subjects with hSBA seroresponse, directed against N. meningitidis serogroups A, C, W and Y.**

|                                                                                                                                                                                                                                                                                                                                                                              |                                                                                                                                                                                            |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                              | To assess the immunogenicity of a single injection of MenACWY as measured by the percentage of subjects with hSBA seroresponse, directed against N. meningitidis serogroups A, C, W and Y. |
| End point description:<br>Seroresponse is defined as: <ul style="list-style-type: none"><li>for subjects with a pre-vaccination hSBA titer &lt; 1:4, a postvaccination hSBA titer <math>\geq</math> 1:8.</li><li>for subjects with a pre-vaccination hSBA titer <math>\geq</math> 1:4, an increase in hSBA titer of at least four times the pre-vaccination titer.</li></ul> |                                                                                                                                                                                            |
| End point type                                                                                                                                                                                                                                                                                                                                                               | Primary                                                                                                                                                                                    |
| End point timeframe:<br>At day 29 post-vaccination.                                                                                                                                                                                                                                                                                                                          |                                                                                                                                                                                            |

| End point values                             | MenACWY-CRM     | Placebo         |  |  |
|----------------------------------------------|-----------------|-----------------|--|--|
| Subject group type                           | Reporting group | Reporting group |  |  |
| Number of subjects analysed                  | 295             | 152             |  |  |
| Units: Percentage of subjects                |                 |                 |  |  |
| number (confidence interval 95%)             |                 |                 |  |  |
| Men A Seroresponse -baseline < 4 (N=246,120) | 76 (70 to 81)   | 2 (0 to 6)      |  |  |

|                                                      |               |               |  |  |
|------------------------------------------------------|---------------|---------------|--|--|
| Men A Seroresponse -baseline $\geq 4$<br>(N=49,32)   | 76 (61 to 87) | 0 (0 to 11)   |  |  |
| Men A Overall Seroresponse<br>(N=295,152)            | 76 (71 to 81) | 1 (0 to 5)    |  |  |
| Men C Seroresponse -baseline $< 4$<br>(N=111,67)     | 96 (91 to 99) | 3 (0 to 10)   |  |  |
| Men C Seroresponse -baseline $\geq 4$<br>(N=182,83)  | 80 (74 to 86) | 0 (0 to 4)    |  |  |
| Men C Overall Seroresponse<br>(N=293,150)            | 86 (82 to 90) | 1 (0 to 5)    |  |  |
| Men W Seroresponse -baseline $< 4$<br>(N=32,20)      | 84 (67 to 95) | 30 (12 to 54) |  |  |
| Men W Seroresponse -baseline $\geq 4$<br>(N=261,131) | 21 (16 to 26) | 0 (0 to 3)    |  |  |
| Men W Overall Seroresponse<br>(N=293,151)            | 28 (23 to 33) | 4 (1 to 8)    |  |  |
| Men Y Seroresponse -baseline $< 4$<br>(N=119,62)     | 89 (82 to 94) | 5 (1 to 13)   |  |  |
| Men Y Seroresponse -baseline $\geq 4$<br>(N=175,90)  | 55 (47 to 62) | 0 (0 to 4)    |  |  |
| Men Y Overall Seroresponse<br>(N=294,152)            | 69 (63 to 74) | 2 (0 to 6)    |  |  |

## Statistical analyses

|                                                                                                                                                                      |                                    |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                    | Immune response in serogroup Men A |
| Statistical analysis description:                                                                                                                                    |                                    |
| Statistical Analysis 1 for Percentages of Subjects With Seroresponse, Directed Against Neisseria Meningitidis Serogroups A, C, W and Y After MenACWY-CRM Vaccination |                                    |
| Comparison groups                                                                                                                                                    | MenACWY-CRM v Placebo              |
| Number of subjects included in analysis                                                                                                                              | 447                                |
| Analysis specification                                                                                                                                               | Pre-specified                      |
| Analysis type                                                                                                                                                        | other                              |
| Method                                                                                                                                                               | Clopper Pearson                    |
| Parameter estimate                                                                                                                                                   | Vaccine group differences          |
| Point estimate                                                                                                                                                       | 75                                 |
| Confidence interval                                                                                                                                                  |                                    |
| level                                                                                                                                                                | 95 %                               |
| sides                                                                                                                                                                | 2-sided                            |
| lower limit                                                                                                                                                          | 69                                 |
| upper limit                                                                                                                                                          | 79                                 |
| Variability estimate                                                                                                                                                 | Standard deviation                 |

|                                                                                                                                                                       |                                     |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                     | Immune response in serogroup Men C. |
| Statistical analysis description:                                                                                                                                     |                                     |
| Statistical Analysis 2 for Percentages of Subjects With Seroresponse, Directed Against Neisseria Meningitidis Serogroups A, C, W and Y After MenACWY-CRM Vaccination. |                                     |
| Comparison groups                                                                                                                                                     | MenACWY-CRM v Placebo               |



|                                         |                           |
|-----------------------------------------|---------------------------|
| Number of subjects included in analysis | 447                       |
| Analysis specification                  | Pre-specified             |
| Analysis type                           | other                     |
| Method                                  | Clopper Pearson           |
| Parameter estimate                      | Vaccine group differences |
| Point estimate                          | 85                        |
| Confidence interval                     |                           |
| level                                   | 95 %                      |
| sides                                   | 2-sided                   |
| lower limit                             | 80                        |
| upper limit                             | 89                        |

|                                                                                                                                                                       |                                     |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                     | Immune response in serogroup Men W. |
| Statistical analysis description:                                                                                                                                     |                                     |
| Statistical Analysis 3 for Percentages of Subjects With Seroresponse, Directed Against Neisseria Meningitidis Serogroups A, C, W and Y After MenACWY-CRM Vaccination. |                                     |
| Comparison groups                                                                                                                                                     | MenACWY-CRM v Placebo               |
| Number of subjects included in analysis                                                                                                                               | 447                                 |
| Analysis specification                                                                                                                                                | Pre-specified                       |
| Analysis type                                                                                                                                                         | other                               |
| Method                                                                                                                                                                | Clopper Pearson                     |
| Parameter estimate                                                                                                                                                    | Vaccine group differences           |
| Point estimate                                                                                                                                                        | 24                                  |
| Confidence interval                                                                                                                                                   |                                     |
| level                                                                                                                                                                 | 95 %                                |
| sides                                                                                                                                                                 | 2-sided                             |
| lower limit                                                                                                                                                           | 18                                  |
| upper limit                                                                                                                                                           | 30                                  |

|                                                                                                                                                                       |                                     |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                     | Immune response in serogroup Men Y. |
| Statistical analysis description:                                                                                                                                     |                                     |
| Statistical Analysis 2 for Percentages of Subjects With Seroresponse, Directed Against Neisseria Meningitidis Serogroups A, C, W and Y After MenACWY-CRM Vaccination. |                                     |
| Comparison groups                                                                                                                                                     | MenACWY-CRM v Placebo               |
| Number of subjects included in analysis                                                                                                                               | 447                                 |
| Analysis specification                                                                                                                                                | Pre-specified                       |
| Analysis type                                                                                                                                                         | other                               |
| Method                                                                                                                                                                | Clopper Pearson                     |
| Parameter estimate                                                                                                                                                    | Vaccine group differences           |
| Point estimate                                                                                                                                                        | 67                                  |
| Confidence interval                                                                                                                                                   |                                     |
| level                                                                                                                                                                 | 95 %                                |
| sides                                                                                                                                                                 | 2-sided                             |
| lower limit                                                                                                                                                           | 61                                  |
| upper limit                                                                                                                                                           | 72                                  |

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**Primary: Number of Subjects Who Reported Local and Systemic Reactogenicity During 7 Days After MenACWY-CRM Vaccination**

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|                 |                                                                                                                              |
|-----------------|------------------------------------------------------------------------------------------------------------------------------|
| End point title | Number of Subjects Who Reported Local and Systemic Reactogenicity During 7 Days After MenACWY-CRM Vaccination <sup>[1]</sup> |
|-----------------|------------------------------------------------------------------------------------------------------------------------------|

End point description:

Numbers of subjects with reported local and systemic reactions and other AEs.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

During 7 days after 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: There was no statistical null hypothesis associated with this safety objective.

| End point values                     | MenACWY-CRM     | Placebo         |  |  |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type                   | Reporting group | Reporting group |  |  |
| Number of subjects analysed          | 297             | 153             |  |  |
| Units: Number of Subjects            |                 |                 |  |  |
| Any Local                            | 83              | 14              |  |  |
| Pain                                 | 69              | 12              |  |  |
| Erythema                             | 30              | 3               |  |  |
| Induration                           | 30              | 0               |  |  |
| Systemic                             | 83              | 43              |  |  |
| Chills                               | 17              | 7               |  |  |
| Nausea                               | 22              | 10              |  |  |
| Myalgia                              | 45              | 13              |  |  |
| Arthralgia                           | 6               | 4               |  |  |
| Headache                             | 39              | 25              |  |  |
| Rash                                 | 1               | 0               |  |  |
| Fever ( $\geq 38^{\circ}\text{C}$ )  | 3               | 1               |  |  |
| Stayed home due to reaction          | 9               | 2               |  |  |
| Analgesic/antipyretic medication use | 7               | 3               |  |  |

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**Statistical analyses**

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No statistical analyses for this end point

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**Secondary: To assess the immunogenicity of MenACWY as measured by the percentage of subjects with hSBA  $\geq 1:8$  directed against N. meningitidis serogroups A, C, W and Y**

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|                 |                                                                                                                                                                  |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | To assess the immunogenicity of MenACWY as measured by the percentage of subjects with hSBA $\geq 1:8$ directed against N. meningitidis serogroups A, C, W and Y |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Percentage of subjects with hSBA  $\geq 1:8$  to N. meningitidis serogroups A, C, W135 and Y.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At day 1 and day 29 post-vaccination.

| End point values                 | MenACWY-CRM     | Placebo         |  |  |
|----------------------------------|-----------------|-----------------|--|--|
| Subject group type               | Reporting group | Reporting group |  |  |
| Number of subjects analysed      | 295             | 152             |  |  |
| Units: Percentages of subjects   |                 |                 |  |  |
| number (confidence interval 95%) |                 |                 |  |  |
| Men A Day 1 (N=295,152)          | 13 (9 to 17)    | 15 (10 to 22)   |  |  |
| Men A Day 29 (N=295,152)         | 79 (74 to 84)   | 16 (10 to 23)   |  |  |
| Men C Day 1 (N=293,150)          | 49 (44 to 55)   | 39 (31 to 47)   |  |  |
| Men C Day 29 (N=293,150)         | 99 (97 to 100)  | 37 (30 to 46)   |  |  |
| Men W Day 1 (N=293,151)          | 89 (85 to 92)   | 87 (80 to 92)   |  |  |
| Men W Day 29 (N=293,151)         | 98 (96 to 99)   | 88 (82 to 93)   |  |  |
| Men Y Day 1 (N=294,152)          | 54 (48 to 60)   | 53 (44 to 61)   |  |  |
| Men Y Day 29 (N=294,152)         | 94 (91 to 97)   | 51 (42 to 59)   |  |  |

### Statistical analyses

No statistical analyses for this end point

**Secondary: To assess the immunogenicity of MenACWY as measured by the hSBA geometric mean titers (GMTs) directed against N. meningitidis serogroups A, C, W and Y.**

|                 |                                                                                                                                                         |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | To assess the immunogenicity of MenACWY as measured by the hSBA geometric mean titers (GMTs) directed against N. meningitidis serogroups A, C, W and Y. |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

Immunogenicity was assessed as hSBA GMTs and associated 95% CI, measured against N. meningitidis serogroups A, C, W and Y, before the vaccination (baseline, day 1) and at day 29 (28 days after MenACWY-CRM vaccination).

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At day 1 and day 29 post-vaccination.

| End point values                         | MenACWY-CRM        | Placebo             |  |  |
|------------------------------------------|--------------------|---------------------|--|--|
| Subject group type                       | Reporting group    | Reporting group     |  |  |
| Number of subjects analysed              | 295                | 152                 |  |  |
| Units: GMT                               |                    |                     |  |  |
| geometric mean (confidence interval 95%) |                    |                     |  |  |
| Men A Day 1 (N=295,152)                  | 2.7 (2.47 to 2.95) | 2.86 (2.53 to 3.24) |  |  |
| Men A Day 29 (N=295,152)                 | 48 (39 to 57)      | 3 (2.31 to 3.88)    |  |  |

|                          |                     |                     |  |  |
|--------------------------|---------------------|---------------------|--|--|
| Men C Day 1 (N=293,150)  | 7.82 (6.76 to 9.05) | 5.94 (4.85 to 7.27) |  |  |
| Men C Day 29 (N=293,150) | 231 (198 to 269)    | 6.04 (4.89 to 7.47) |  |  |
| Men W Day 1 (N=293,151)  | 51 (44 to 61)       | 48 (38 to 60)       |  |  |
| Men W Day 29 (N=293,151) | 147 (125 to 171)    | 47 (38 to 58)       |  |  |
| Men Y Day 1 (N=294,152)  | 9.01 (7.64 to 11)   | 8.82 (7.02 to 11)   |  |  |
| Men Y Day 29 (N=294,152) | 107 (89 to 128)     | 8.4 (6.54 to 11)    |  |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Solicited local and systemic AEs, oral temperature, all other AEs, and all concomitant medications were collected for 7 days following each vaccination. SAEs and AEs leading to withdrawal from the study were collected throughout the entire study period.

Adverse event reporting additional description:

Analysis was done on safety population ie, the subjects in the exposed population who provided post-baseline safety data.

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 14.0 |
|--------------------|------|

### Reporting groups

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description:

Subjects received the saline placebo

|                       |             |
|-----------------------|-------------|
| Reporting group title | MenACWY-CRM |
|-----------------------|-------------|

Reporting group description:

Subjects received one dose of MenACWY-CRM conjugate vaccine

| Serious adverse events                            | Placebo         | MenACWY-CRM     |  |
|---------------------------------------------------|-----------------|-----------------|--|
| Total subjects affected by serious adverse events |                 |                 |  |
| subjects affected / exposed                       | 0 / 153 (0.00%) | 0 / 297 (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                            | Placebo                                                              | MenACWY-CRM        |  |
|-------------------------------------------------------|----------------------------------------------------------------------|--------------------|--|
| Total subjects affected by non-serious adverse events |                                                                      |                    |  |
| subjects affected / exposed                           | 50 / 153 (32.68%)                                                    | 117 / 297 (39.39%) |  |
| Nervous system disorders                              |                                                                      |                    |  |
| Headache                                              | Additional description: For Occurences MedDRA 17.1 version was used  |                    |  |
| subjects affected / exposed                           | 25 / 153 (16.34%)                                                    | 39 / 297 (13.13%)  |  |
| occurrences (all)                                     | 27                                                                   | 48                 |  |
| General disorders and administration site conditions  |                                                                      |                    |  |
| Chills                                                | Additional description: For occurences MedDRA 17.1 version was used. |                    |  |

|                                                 |                                                                      |                   |  |
|-------------------------------------------------|----------------------------------------------------------------------|-------------------|--|
| subjects affected / exposed                     | 7 / 153 (4.58%)                                                      | 17 / 297 (5.72%)  |  |
| occurrences (all)                               | 8                                                                    | 22                |  |
| Injection site erythema                         | Additional description: For occurrences MedDRA 17.1 version was used |                   |  |
| subjects affected / exposed                     | 3 / 153 (1.96%)                                                      | 30 / 297 (10.10%) |  |
| occurrences (all)                               | 3                                                                    | 30                |  |
| Injection site induration                       | Additional description: For Occurences MedDRA 17.1 version was used  |                   |  |
| subjects affected / exposed                     | 0 / 153 (0.00%)                                                      | 30 / 297 (10.10%) |  |
| occurrences (all)                               | 0                                                                    | 30                |  |
| Injection site pain                             | Additional description: For Occurences MedDRA 17.1 version was used  |                   |  |
| subjects affected / exposed                     | 12 / 153 (7.84%)                                                     | 69 / 297 (23.23%) |  |
| occurrences (all)                               | 12                                                                   | 72                |  |
| Malaise                                         | Additional description: For Occurences MedDRA 17.1 version was used  |                   |  |
| subjects affected / exposed                     | 9 / 153 (5.88%)                                                      | 21 / 297 (7.07%)  |  |
| occurrences (all)                               | 9                                                                    | 23                |  |
| Gastrointestinal disorders                      |                                                                      |                   |  |
| Nausea                                          | Additional description: For Occurences MedDRA 17.1 version was used  |                   |  |
| subjects affected / exposed                     | 10 / 153 (6.54%)                                                     | 22 / 297 (7.41%)  |  |
| occurrences (all)                               | 11                                                                   | 27                |  |
| Musculoskeletal and connective tissue disorders |                                                                      |                   |  |
| Myalgia                                         | Additional description: For Occurences MedDRA 17.1 version was used  |                   |  |
| subjects affected / exposed                     | 13 / 153 (8.50%)                                                     | 46 / 297 (15.49%) |  |
| occurrences (all)                               | 15                                                                   | 50                |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment                                                                                                                                                                                                                                                                              |
|------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 15 November 2010 | This single amendment to the original protocol was implemented to clarify AE relatedness definitions and to correct the way indications of rash are captured. None of the revisions significantly altered the study conduct or would influence the interpretation of the study results |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported