



## Clinical trial results:

### A Phase 2b, Open-Label, Multi-Center Study to Evaluate the Persistence of Antibody Response and to Assess the Immune Response to a Booster Dose of MenACWY Conjugate Vaccine in Subjects Previously Vaccinated as Adolescents with Either MenACWY Conjugate Vaccine or Menomune®

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

## Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2014-005059-25 |
| Trial protocol           | Outside EU/EEA |
| Global end of trial date | 25 July 2010   |

## Results information

|                                |   |
|--------------------------------|---|
| Result version number          | v2 (current)  |
| This version publication date  | 04 June 2016  |
| First version publication date | 18 March 2015   |
| Version creation reason        | <ul style="list-style-type: none"><li>• Correction of full data set re-QC needed to study because of EudraCT system glitch and updates to results are required.</li></ul> |

## Trial information

### Trial identification

|                       |         |
|-----------------------|---------|
| Sponsor protocol code | V59P6E1 |
|-----------------------|---------|

### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01018732 |
| WHO universal trial number (UTN)   | -           |

Notes:

## Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | Novartis Vaccines and Diagnostics Inc.  |
| Sponsor organisation address | 350 Massachusetts Ave, Cambridge, United States, 02139  |
| Public contact               | Posting Director, Novartis Vaccines and Diagnostics Inc.,<br>RegistryContactVaccinesUS@novartis.com |
| Scientific contact           | Posting Director, Novartis Vaccines and Diagnostics Inc.,<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                       | 09 June 2011 |
| Is this the analysis of the primary completion data? | No           |
| Global end of trial reached?                         | Yes          |
| Global end of trial date                             | 25 July 2010 |
| Was the trial ended prematurely?                     | No           |

Notes:

## General information about the trial

Main objective of the trial:

1. To evaluate the persistence of the antibody response at 5 years after one dose of MenACWY or Menomune®, as measured by the percentage of subjects with bactericidal activity using human complement (hSBA)  $\geq 1:8$  directed against N. meningitidis serogroups A, C, W-135, and Y.
2. To evaluate the antibody response to one dose of MenACWY in subjects who had previously received one dose of MenACWY compared to the antibody response to one dose of MenACWY in meningococcal vaccine-naïve subjects, as measured by hSBA geometric mean titers (GMTs) directed against N. meningitidis serogroups A, C, W-135 and Y, at 28 days after vaccination.

Protection of trial subjects:

This clinical study was designed, implemented and reported in accordance with the International Conference on Harmonization (ICH) Harmonized Tripartite Guidelines for Good Clinical Practice (GCP), with applicable local regulations (including European Directive 2001/20/EC, US Code of Federal Regulations Title 21, and Japanese Ministry of Health, Labor, and Welfare), and with the ethical principles laid down in the Declaration of Helsinki.

Background therapy:

N/A

Evidence for comparator:

N/A

|   |                 |
|---|-----------------|
| Actual start date of recruitment                          | 19 January 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 | United States: 155 |
| Worldwide total number of subjects   | 155                |
| 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)                    | 0   |
| Adolescents (12-17 years)                | 38  |
| Adults (18-64 years)                     | 117 |
| From 65 to 84 years                      | 0   |
| 85 years and over                        | 0   |

## Subject disposition

### Recruitment

Recruitment details:

Subjects were enrolled at 3 centers in the US.

### Pre-assignment

Screening details:

All subjects enrolled were included in the trial.

### Period 1

|                              |                                 |
|------------------------------|---------------------------------|
| Period 1 title               | Overall Period (overall period) |
| Is this the baseline period? | Yes                             |
| Allocation method            | Non-randomised - controlled     |
| Blinding used                | Not blinded                     |

Blinding implementation details:

The trial was designed as an open-label study; all subjects received the same vaccine, their allocation had been previously revealed to the sites after unblinding of the parent study. Subjects, investigators, and other study personnel were not blinded. The only personnel who were blinded were the data analysts and the laboratory personnel who received the sera.

### Arms

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

Arm description:

Subjects had been given one dose of Meningococcal (groups A, C, W, and Y) vaccine conjugated to CRM197 (cross-reactive material-mutant of diphtheria toxin) (MenACWY) 5 years ago.

|  |  |
|--|--|
| Arm type                               | Experimental                                   |
| Investigational medicinal product name | MenACWY  |
| Investigational medicinal product code | N/A  |
| Other name                             |  |
| Pharmaceutical forms                   | Powder and solution for solution for injection |
| Routes of administration               | Intramuscular use                              |

Dosage and administration details:

One dose of 0.5mL.

|                  |   |
|------------------|---|
| <b>Arm title</b> | Licensed Polysaccharide Meningococcal Vaccine |
|------------------|---|

Arm description:

Subjects had been given one dose of licensed Men ACWY (Menomune®) 5 years ago.

|  |  |
|--|--|
| Arm type                               | Experimental                                   |
| Investigational medicinal product name | MenACWY  |
| Investigational medicinal product code | N/A  |
| Other name                             |  |
| Pharmaceutical forms                   | Powder and solution for solution for injection |
| Routes of administration               | Intramuscular use                              |

Dosage and administration details:

One dose of 0.5mL.

|                  |                     |
|------------------|---------------------|
| <b>Arm title</b> | Meningococcal Naïve |
|------------------|---------------------|

Arm description:

Subjects were between 16 years to 23 years (age-inclusive) and meningococcal vaccine naïve.

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

|  |  |
|--|--|
| Investigational medicinal product name | MenACWY  |
| Investigational medicinal product code | N/A  |
| Other name                             |  |
| Pharmaceutical forms                   | Powder and solution for solution for injection |
| Routes of administration               | Intramuscular use                              |

Dosage and administration details:

One dose of 0.5mL.

| Number of subjects in period 1 | MenACWY-CRM Vaccine | Licensed Polysaccharide Meningococcal Vaccine | Meningococcal Naïve |
|--------------------------------|---------------------|---|---------------------|
|                                |                     |   |                     |
| Started                        | 50                  | 51  | 54                  |
| Completed                      | 49                  | 49  | 50                  |
| Not completed                  | 1                   | 2   | 4                   |
| Unable to classify             | -                   | -   | 1                   |
| Inappropriate enrolment        | -                   | 1   | -                   |
| Lost to follow-up              | -                   | -   | 3                   |
| Protocol deviation             | 1                   | 1   | -                   |

## Baseline characteristics

### Reporting groups

|  |   |
|--|---|
| Reporting group title  | MenACWY-CRM Vaccine                           |
| Reporting group description:<br>Subjects had been given one dose of Meningococcal (groups A, C, W, and Y) vaccine conjugated to CRM197 (cross-reactive material-mutant of diphtheria toxin) (MenACWY) 5 years ago. |   |
| Reporting group title  | Licensed Polysaccharide Meningococcal Vaccine |
| Reporting group description:<br>Subjects had been given one dose of licensed Men ACWY (Menomune®) 5 years ago.   |   |
| Reporting group title  | Meningococcal Naïve                           |
| Reporting group description:<br>Subjects were between 16 years to 23 years (age-inclusive) and meningococcal vaccine naïve.  |   |

| Reporting group values  | MenACWY-CRM Vaccine | Licensed Polysaccharide Meningococcal Vaccine | Meningococcal Naïve |
|---|---------------------|---|---------------------|
| Number of subjects  | 50                  | 51  | 54                  |
| Age categorical<br>Units: Subjects  |                     |   |                     |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years)<br>Adolescents (12-17 years)<br>Adults (18-64 years)<br>From 65-84 years<br>85 years and over |                     |   |                     |
| Age continuous<br>Units: years  |                     |   |                     |
| arithmetic mean   | 18.8                | 19.2  | 20.5                |
| standard deviation  | ± 1.9               | ± 2   | ± 2.3               |
| Gender categorical<br>Units: Subjects   |                     |   |                     |
| Female  | 22                  | 28  | 33                  |
| Male  | 28                  | 23  | 21                  |

| Reporting group values  | Total                 |  |  |
|---|-----------------------|--|--|
| Number of subjects  | 155                   |  |  |
| Age categorical<br>Units: Subjects  |                       |  |  |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years) | 0<br>0<br>0<br>0<br>0 |  |  |

|   |    |  |  |
|---|----|--|--|
| Adolescents (12-17 years)   | 0  |  |  |
| Adults (18-64 years)  | 0  |  |  |
| From 65-84 years  | 0  |  |  |
| 85 years and over   | 0  |  |  |
| Age continuous<br>Units: years<br>arithmetic mean<br>standard deviation | -  |  |  |
| Gender categorical<br>Units: Subjects                                   |    |  |  |
| Female  | 83 |  |  |
| Male  | 72 |  |  |

## Subject analysis sets

|   |   |
|---|---|
| Subject analysis set title  | Exposed Population  |
| Subject analysis set type   | Intention-to-treat  |
| Subject analysis set description:<br>All enrolled subjects who actually received the study vaccination.   |   |
| Subject analysis set title  | Enrolled Population   |
| Subject analysis set type   | Intention-to-treat  |
| Subject analysis set description:<br>All subjects who signed an informed consent and underwent screening procedure(s).  |   |
| Subject analysis set title  | FAS, Immunogenicity after one dose of MenACWY (FAS Booster) |
| Subject analysis set type   | Full analysis   |
| Subject analysis set description:<br>All subjects who received the study vaccination, and provided at least one evaluable serum sample before or after baseline and whose assay result is available for at least one serogroup. |   |
| Subject analysis set title  | Full Analysis Set, Antibody Persistence (FAS Persist)       |
| Subject analysis set type   | Full analysis   |
| Subject analysis set description:<br>All subjects in the enrolled population with an evaluable blood sample at day 1 and whose assay result was available for at least one serogroup.   |   |
| Subject analysis set title  | Safety Population   |
| Subject analysis set type   | Safety analysis   |
| Subject analysis set description:<br>All subjects in the Exposed Population who provided post-baseline safety data.   |   |

| Reporting group values  | Exposed Population | Enrolled Population | FAS, Immunogenicity after one dose of MenACWY (FAS Booster) |
|---|--------------------|---------------------|---|
| Number of subjects  | 153                | 155                 | 148   |
| Age categorical<br>Units: Subjects  |                    |                     |   |
| In utero<br>Preterm newborn infants (gestational age < 37 wks)<br>Newborns (0-27 days)<br>Infants and toddlers (28 days-23 months)<br>Children (2-11 years) |                    |                     |   |

|                           |   |       |   |
|---------------------------|---|-------|---|
| Adolescents (12-17 years) |   |       |   |
| Adults (18-64 years)      |   |       |   |
| From 65-84 years          |   |       |   |
| 85 years and over         |   |       |   |
| Age continuous            |   |       |   |
| Units: years              |   |       |   |
| arithmetic mean           |   | 19.5  |   |
| standard deviation        | ± | ± 2.1 | ± |
| Gender categorical        |   |       |   |
| Units: Subjects           |   |       |   |
| Female                    |   | 83    |   |
| Male                      |   | 72    |   |

| <b>Reporting group values</b>                         | Full Analysis Set,<br>Antibody Persistence<br>(FAS Persist) | Safety Population |  |
|---|---|-------------------|--|
| Number of subjects                                    | 153   | 153               |  |
| Age categorical                                       |   |                   |  |
| Units: Subjects                                       |   |                   |  |
| In utero  |   |                   |  |
| Preterm newborn infants<br>(gestational age < 37 wks) |   |                   |  |
| Newborns (0-27 days)                                  |   |                   |  |
| Infants and toddlers (28 days-23<br>months)           |   |                   |  |
| Children (2-11 years)                                 |   |                   |  |
| Adolescents (12-17 years)                             |   |                   |  |
| Adults (18-64 years)                                  |   |                   |  |
| From 65-84 years                                      |   |                   |  |
| 85 years and over                                     |   |                   |  |
| Age continuous  |   |                   |  |
| Units: years  |   |                   |  |
| arithmetic mean                                       |   |                   |  |
| standard deviation                                    | ±   | ±                 |  |
| Gender categorical                                    |   |                   |  |
| Units: Subjects                                       |   |                   |  |
| Female  |   |                   |  |
| Male  |   |                   |  |



## End points

### End points reporting groups

|   |   |
|---|---|
| Reporting group title   | MenACWY-CRM Vaccine   |
| Reporting group description:<br>Subjects had been given one dose of Meningococcal (groups A, C, W, and Y) vaccine conjugated to CRM197 (cross-reactive material-mutant of diphtheria toxin) (MenACWY) 5 years ago.              |   |
| Reporting group title   | Licensed Polysaccharide Meningococcal Vaccine               |
| Reporting group description:<br>Subjects had been given one dose of licensed Men ACWY (Menomune®) 5 years ago.  |   |
| Reporting group title   | Meningococcal Naïve   |
| Reporting group description:<br>Subjects were between 16 years to 23 years (age-inclusive) and meningococcal vaccine naïve.   |   |
| Subject analysis set title  | Exposed Population  |
| Subject analysis set type   | Intention-to-treat  |
| Subject analysis set description:<br>All enrolled subjects who actually received the study vaccination.   |   |
| Subject analysis set title  | Enrolled Population   |
| Subject analysis set type   | Intention-to-treat  |
| Subject analysis set description:<br>All subjects who signed an informed consent and underwent screening procedure(s).  |   |
| Subject analysis set title  | FAS, Immunogenicity after one dose of MenACWY (FAS Booster) |
| Subject analysis set type   | Full analysis   |
| Subject analysis set description:<br>All subjects who received the study vaccination, and provided at least one evaluable serum sample before or after baseline and whose assay result is available for at least one serogroup. |   |
| Subject analysis set title  | Full Analysis Set, Antibody Persistence (FAS Persist)       |
| Subject analysis set type   | Full analysis   |
| Subject analysis set description:<br>All subjects in the enrolled population with an evaluable blood sample at day 1 and whose assay result was available for at least one serogroup.   |   |
| Subject analysis set title  | Safety Population   |
| Subject analysis set type   | Safety analysis   |
| Subject analysis set description:<br>All subjects in the Exposed Population who provided post-baseline safety data.   |   |

### Primary: 1. Percentages of Subjects With Serum Bactericidal Activity $\geq 8$ at 5 Years After Primary Vaccination

|   |  |
|---|--|
| End point title   | 1. Percentages of Subjects With Serum Bactericidal Activity $\geq 8$ at 5 Years After Primary Vaccination <sup>[1]</sup> |
| End point description:<br>Persistence of antibody response was measured by the percentages of subjects who showed hSBA $\geq 8$ [i.e. percentages of subjects with hSBA titer $\geq 8$ ] in previously vaccinated subjects and in age-matched meningococcal vaccine naïve subjects. Sera were tested against Neisseria meningitidis (N. Meningitidis) serogroups A, C, W-135 and Y.<br>The analysis was done on the FAS, Antibody Persistence Population. |  |
| End point type  | Primary  |
| End point timeframe:<br>Day 1 (5 years after primary 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: No statistical analysis is associated to this endpoint. Analyses were run descriptively.

| End point values                 | MenACWY-CRM Vaccine | Licensed Polysaccharide Meningococcal Vaccine | Meningococcal Naïve |  |
|----------------------------------|---------------------|---|---------------------|--|
| Subject group type               | Reporting group     | Reporting group                               | Reporting group     |  |
| Number of subjects analysed      | 50                  | 50  | 53                  |  |
| Units: Percentages of Subjects   |                     |   |                     |  |
| number (confidence interval 95%) |                     |   |                     |  |
| Men A                            | 30 (18 to 45)       | 44 (30 to 59)                                 | 11 (4 to 23)        |  |
| Men C                            | 76 (62 to 87)       | 62 (47 to 75)                                 | 51 (37 to 65)       |  |
| Men W-135                        | 72 (58 to 84)       | 56 (41 to 70)                                 | 51 (37 to 65)       |  |
| Men Y                            | 76 (62 to 87)       | 50 (36 to 64)                                 | 55 (40 to 68)       |  |

## Statistical analyses

No statistical analyses for this end point

## Primary: 2. Geometric Mean Titer After Booster Vaccination

|                 |   |
|-----------------|---|
| End point title | 2. Geometric Mean Titer After Booster Vaccination |
|-----------------|---|

End point description:

Immunogenicity was measured by hSBA and reported as hSBA Geometric Mean Titer (GMT) in previously vaccinated subjects and in age-matched meningococcal vaccine-naïve subjects. Sera was tested against *Neisseria meningitidis* serogroups A, C, W-135 and Y.

The analysis was done on the FAS, Immunogenicity after one dose of MenACWY (FAS Booster) Population.

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

End point timeframe:

Day 8, Day 29 (after a booster at 5 years after primary vaccination).

| End point values                         | MenACWY-CRM Vaccine | Licensed Polysaccharide Meningococcal Vaccine | Meningococcal Naïve |  |
|--|---------------------|---|---------------------|--|
| Subject group type                       | Reporting group     | Reporting group                               | Reporting group     |  |
| Number of subjects analysed              | 49                  | 49  | 50                  |  |
| Units: Titers                            |                     |   |                     |  |
| geometric mean (confidence interval 95%) |                     |   |                     |  |
| Baseline, Men A                          | 5.16 (3.46 to 7.7)  | 7.31 (4.94 to 11)                             | 3.06 (2.06 to 4.55) |  |
| Day 8, Men A                             | 1059 (585 to 1917)  | 45 (25 to 80)                                 | 34 (19 to 61)       |  |
| Day 29, Men A, (N=48, 49, 50)            | 819 (514 to 1305)   | 147 (94 to 232)                               | 113 (72 to 179)     |  |
| Baseline, Men C                          | 20 (13 to 33)       | 19 (12 to 31)                                 | 7.34 (4.6 to 12)    |  |

|                              |                     |                  |                   |  |
|------------------------------|---------------------|------------------|-------------------|--|
| Day 8, Men C                 | 1603 (893 to 2877)  | 36 (20 to 64)    | 70 (39 to 124)    |  |
| Day 29, Men C                | 1217 (717 to 2066)  | 51 (30 to 86)    | 127 (75 to 214)   |  |
| Baseline, Men W-135          | 29 (17 to 49)       | 12 (7.02 to 19)  | 11 (6.31 to 18)   |  |
| Day 8, Men W-135             | 1685 (1042 to 2725) | 34 (21 to 54)    | 63 (39 to 101)    |  |
| Day 29, Men W-135            | 1644 (1090 to 2481) | 47 (32 to 71)    | 79 (52 to 118)    |  |
| Baseline, Men Y              | 28 (18 to 45)       | 7.8 (4.91 to 12) | 8.69 (5.45 to 14) |  |
| Day 8, Men Y, (N=48, 49, 50) | 2561 (1526 to 4298) | 21 (13 to 35)    | 64 (39 to 107)    |  |
| Day 29, Men Y                | 2092 (1340 to 3268) | 63 (41 to 98)    | 110 (70 to 170)   |  |

## Statistical analyses

| Statistical analysis title  | Statistical Analysis 1 for GMT After Booster                        |
|---|---|
| Statistical analysis description:<br>Day 1 (Pre-booster), Men A, Pairwise comparison of geometric mean titer. |   |
| Comparison groups   | Meningococcal Naïve v Licensed Polysaccharide Meningococcal Vaccine |
| Number of subjects included in analysis   | 99  |
| Analysis specification  | Pre-specified   |
| Analysis type   | other   |
| Method  | ANOVA   |
| Parameter estimate  | Vaccine Group Ratios  |
| Point estimate  | 2.39  |
| Confidence interval   |   |
| level   | 95 %  |
| sides   | 2-sided   |
| lower limit   | 1.39  |
| upper limit   | 4.1   |

| Statistical analysis title  | Statistical Analysis 2 for GMT After Booster                        |
|---|---|
| Statistical analysis description:<br>Day 1 (Pre-booster), Men A, Pairwise comparison of geometric mean titer. |   |
| Comparison groups   | Licensed Polysaccharide Meningococcal Vaccine v MenACWY-CRM Vaccine |
| Number of subjects included in analysis   | 98  |
| Analysis specification  | Pre-specified   |
| Analysis type   | other   |
| Method  | ANOVA   |
| Parameter estimate  | Vaccine Group Ratios  |
| Point estimate  | 0.71  |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 95 %    |
| sides               | 2-sided |
| lower limit         | 0.42    |
| upper limit         | 1.2     |

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Statistical Analysis 3 for GMT After Booster |
| Statistical analysis description:  |  |
| Day 1 (Pre-booster), Men A, Pairwise comparison of geometric mean titer. |  |
| Comparison groups  | Meningococcal Naïve v MenACWY-CRM Vaccine    |
| Number of subjects included in analysis                                  | 99   |
| Analysis specification   | Pre-specified                                |
| Analysis type  | other  |
| Method   | ANOVA  |
| Parameter estimate   | Vaccine Group Ratios                         |
| Point estimate   | 1.68   |
| Confidence interval  |  |
| level  | 95 %   |
| sides  | 2-sided                                      |
| lower limit  | 0.98   |
| upper limit  | 2.9  |

|  |   |
|--|---|
| <b>Statistical analysis title</b>                          | Statistical Analysis 4 for GMT After Booster                        |
| Statistical analysis description:                          |   |
| Day 8, Men A, Pairwise comparison of geometric mean titer. |   |
| Comparison groups  | Meningococcal Naïve v Licensed Polysaccharide Meningococcal Vaccine |
| Number of subjects included in analysis                    | 99  |
| Analysis specification                                     | Pre-specified   |
| Analysis type  | other   |
| Method   | ANOVA   |
| Parameter estimate   | Vaccine Group Ratios  |
| Point estimate   | 1.31  |
| Confidence interval  |   |
| level  | 95 %  |
| sides  | 2-sided   |
| lower limit  | 0.59  |
| upper limit  | 2.91  |

|  |   |
|--|---|
| <b>Statistical analysis title</b>                          | Statistical Analysis 5 for GMT After Booster                        |
| Statistical analysis description:                          |   |
| Day 8, Men A, Pairwise comparison of geometric mean titer. |   |
| Comparison groups  | Licensed Polysaccharide Meningococcal Vaccine v MenACWY-CRM Vaccine |

|   |                      |
|---|----------------------|
| Number of subjects included in analysis | 98                   |
| Analysis specification                  | Pre-specified        |
| Analysis type                           | other                |
| Method                                  | ANOVA                |
| Parameter estimate                      | Vaccine Group Ratios |
| Point estimate                          | 24                   |
| Confidence interval                     |                      |
| level                                   | 95 %                 |
| sides                                   | 2-sided              |
| lower limit                             | 11                   |
| upper limit                             | 52                   |

|   |  |
|---|--|
| <b>Statistical analysis title</b>   | Statistical Analysis 6 for GMT After Booster |
| Statistical analysis description:<br>Day 8, Men A, Pairwise comparison of geometric mean titer. |  |
| Comparison groups   | MenACWY-CRM Vaccine v Meningococcal Naïve    |
| Number of subjects included in analysis   | 99   |
| Analysis specification  | Pre-specified                                |
| Analysis type   | other  |
| Method  | ANOVA  |
| Parameter estimate  | Vaccine Group Ratios                         |
| Point estimate  | 31   |
| Confidence interval   |  |
| level   | 95 %   |
| sides   | 2-sided                                      |
| lower limit   | 14   |
| upper limit   | 69   |

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Statistical Analysis 7 for GMT After Booster                        |
| Statistical analysis description:<br>Day 29, Men A, Pairwise comparison of geometric mean titer. |   |
| Comparison groups  | Meningococcal Naïve v Licensed Polysaccharide Meningococcal Vaccine |
| Number of subjects included in analysis  | 99  |
| Analysis specification   | Pre-specified   |
| Analysis type  | other   |
| Method   | ANOVA   |
| Parameter estimate   | Vaccine Group Ratios  |
| Point estimate   | 1.3   |
| Confidence interval  |   |
| level  | 95 %  |
| sides  | 2-sided   |
| lower limit  | 0.7   |
| upper limit  | 2.42  |

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Statistical Analysis 8 for GMT After Booster                        |
| Statistical analysis description:<br>Day 29, Men A, Pairwise comparison of geometric mean titer. |   |
| Comparison groups  | Licensed Polysaccharide Meningococcal Vaccine v MenACWY-CRM Vaccine |
| Number of subjects included in analysis  | 98  |
| Analysis specification   | Pre-specified   |
| Analysis type  | other   |
| Method   | ANOVA   |
| Parameter estimate   | Vaccine Group Ratios  |
| Point estimate   | 5.56  |
| Confidence interval  |   |
| level  | 95 %  |
| sides  | 2-sided   |
| lower limit  | 3.01  |
| upper limit  | 10  |

|  |  |
|--|--|
| <b>Statistical analysis title</b>  | Statistical Analysis 9 for GMT After Booster |
| Statistical analysis description:<br>Day 29, Men A, Pairwise comparison of geometric mean titer. |  |
| Comparison groups  | MenACWY-CRM Vaccine v Meningococcal Naïve    |
| Number of subjects included in analysis  | 99   |
| Analysis specification   | Pre-specified                                |
| Analysis type  | other  |
| Method   | ANOVA  |
| Parameter estimate   | Vaccine Group Ratios                         |
| Point estimate   | 7.22   |
| Confidence interval  |  |
| level  | 95 %   |
| sides  | 2-sided                                      |
| lower limit  | 3.86   |
| upper limit  | 13   |

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Statistical Analysis 10 for GMT After Booster                       |
| Statistical analysis description:<br>Day 1 (Pre-booster), Men C, Pairwise comparison of geometric mean titer. |   |
| Comparison groups   | Meningococcal Naïve v Licensed Polysaccharide Meningococcal Vaccine |

|   |                      |
|---|----------------------|
| Number of subjects included in analysis | 99                   |
| Analysis specification                  | Pre-specified        |
| Analysis type                           | other                |
| Method                                  | ANOVA                |
| Parameter estimate                      | Vaccine Group Ratios |
| Point estimate                          | 2.64                 |
| Confidence interval                     |                      |
| level                                   | 95 %                 |
| sides                                   | 2-sided              |
| lower limit                             | 1.4                  |
| upper limit                             | 4.99                 |

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Statistical Analysis 11 for GMT After Booster                       |
| Statistical analysis description:<br>Day 1 (Pre-booster), Men C, Pairwise comparison of geometric mean titer. |   |
| Comparison groups   | Licensed Polysaccharide Meningococcal Vaccine v MenACWY-CRM Vaccine |
| Number of subjects included in analysis   | 98  |
| Analysis specification  | Pre-specified   |
| Analysis type   | other   |
| Method  | ANOVA   |
| Parameter estimate  | Vaccine Group Ratios  |
| Point estimate  | 1.05  |
| Confidence interval   |   |
| level   | 95 %  |
| sides   | 2-sided   |
| lower limit   | 0.56  |
| upper limit   | 1.97  |

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Statistical Analysis 12 for GMT After Booster |
| Statistical analysis description:<br>Day 1 (Pre-booster), Men C, Pairwise comparison of geometric mean titer. |   |
| Comparison groups   | MenACWY-CRM Vaccine v Meningococcal Naïve     |
| Number of subjects included in analysis   | 99  |
| Analysis specification  | Pre-specified                                 |
| Analysis type   | other   |
| Method  | ANOVA   |
| Parameter estimate  | Vaccine Group Ratios                          |
| Point estimate  | 2.78  |
| Confidence interval   |   |
| level   | 95 %  |
| sides   | 2-sided                                       |
| lower limit   | 1.47  |
| upper limit   | 5.27  |

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Statistical Analysis 13 for GMT After Booster                       |
| Statistical analysis description:<br>Day 8, Men C, Pairwise comparison of geometric mean titer. |   |
| Comparison groups   | Meningococcal Naïve v Licensed Polysaccharide Meningococcal Vaccine |
| Number of subjects included in analysis   | 99  |
| Analysis specification  | Pre-specified   |
| Analysis type   | other   |
| Method  | ANOVA   |
| Parameter estimate  | Vaccine Group Ratios  |
| Point estimate  | 0.52  |
| Confidence interval   |   |
| level   | 95 %  |
| sides   | 2-sided   |
| lower limit   | 0.23  |
| upper limit   | 1.13  |

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Statistical Analysis 14 for GMT After Booster                       |
| Statistical analysis description:<br>Day 8, Men C, Pairwise comparison of geometric mean titer. |   |
| Comparison groups   | MenACWY-CRM Vaccine v Licensed Polysaccharide Meningococcal Vaccine |
| Number of subjects included in analysis   | 98  |
| Analysis specification  | Pre-specified   |
| Analysis type   | other   |
| Method  | ANOVA   |
| Parameter estimate  | Vaccine Group Ratios  |
| Point estimate  | 45  |
| Confidence interval   |   |
| level   | 95 %  |
| sides   | 2-sided   |
| lower limit   | 21  |
| upper limit   | 97  |

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Statistical Analysis 15 for GMT After Booster |
| Statistical analysis description:<br>Day 8, Men C, Pairwise comparison of geometric mean titer. |   |
| Comparison groups   | Meningococcal Naïve v MenACWY-CRM Vaccine     |



|   |                      |
|---|----------------------|
| Number of subjects included in analysis | 99                   |
| Analysis specification                  | Pre-specified        |
| Analysis type                           | other                |
| Method                                  | ANOVA                |
| Parameter estimate                      | Vaccine Group Ratios |
| Point estimate                          | 23                   |
| Confidence interval                     |                      |
| level                                   | 95 %                 |
| sides                                   | 2-sided              |
| lower limit                             | 10                   |
| upper limit                             | 51                   |

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Statistical Analysis 16 for GMT After Booster                       |
| Statistical analysis description:<br>Day 29, Men C, Pairwise comparison of geometric mean titer. |   |
| Comparison groups  | Meningococcal Naïve v Licensed Polysaccharide Meningococcal Vaccine |
| Number of subjects included in analysis  | 99  |
| Analysis specification   | Pre-specified   |
| Analysis type  | other   |
| Method   | ANOVA   |
| Parameter estimate   | Vaccine Group Ratios  |
| Point estimate   | 0.4   |
| Confidence interval  |   |
| level  | 95 %  |
| sides  | 2-sided   |
| lower limit  | 0.2   |
| upper limit  | 0.82  |

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Statistical Analysis 17 for GMT After Booster                       |
| Statistical analysis description:<br>Day 29, Men C, Pairwise comparison of geometric mean titer. |   |
| Comparison groups  | Licensed Polysaccharide Meningococcal Vaccine v MenACWY-CRM Vaccine |
| Number of subjects included in analysis  | 98  |
| Analysis specification   | Pre-specified   |
| Analysis type  | other   |
| Method   | ANOVA   |
| Parameter estimate   | Vaccine Group Ratios  |
| Point estimate   | 24  |
| Confidence interval  |   |
| level  | 95 %  |
| sides  | 2-sided   |
| lower limit  | 12  |
| upper limit  | 48  |

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Statistical Analysis 18 for GMT After Booster |
| Statistical analysis description:<br>Day 29, Men C, Pairwise comparison of geometric mean titer. |   |
| Comparison groups  | MenACWY-CRM Vaccine v Meningococcal Naïve     |
| Number of subjects included in analysis  | 99  |
| Analysis specification   | Pre-specified                                 |
| Analysis type  | other   |
| Method   | ANOVA   |
| Parameter estimate   | Vaccine Group Ratios                          |
| Point estimate   | 9.61  |
| Confidence interval  |   |
| level  | 95 %  |
| sides  | 2-sided                                       |
| lower limit  | 4.69  |
| upper limit  | 20  |

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Statistical Analysis 19 for GMT After Booster                       |
| Statistical analysis description:<br>Day 1 (Pre-booster), Men W-135, Pairwise comparison of geometric mean titer. |   |
| Comparison groups   | Meningococcal Naïve v Licensed Polysaccharide Meningococcal Vaccine |
| Number of subjects included in analysis   | 99  |
| Analysis specification  | Pre-specified   |
| Analysis type   | other   |
| Method  | ANOVA   |
| Parameter estimate  | Vaccine Group Ratios  |
| Point estimate  | 1.11  |
| Confidence interval   |   |
| level   | 95 %  |
| sides   | 2-sided   |
| lower limit   | 0.55  |
| upper limit   | 2.21  |

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Statistical Analysis 20 for GMT After Booster                       |
| Statistical analysis description:<br>Day 1 (Pre-booster), Men W-135, Pairwise comparison of geometric mean titer. |   |
| Comparison groups   | Licensed Polysaccharide Meningococcal Vaccine v MenACWY-CRM Vaccine |

|   |                      |
|---|----------------------|
| Number of subjects included in analysis | 98                   |
| Analysis specification                  | Pre-specified        |
| Analysis type                           | other                |
| Method                                  | ANOVA                |
| Parameter estimate                      | Vaccine Group Ratios |
| Point estimate                          | 2.51                 |
| Confidence interval                     |                      |
| level                                   | 95 %                 |
| sides                                   | 2-sided              |
| lower limit                             | 1.27                 |
| upper limit                             | 4.96                 |

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Statistical Analysis 21 for GMT After Booster |
| Statistical analysis description:  |   |
| Day 1 (Pre-booster), Men W-135, Pairwise comparison of geometric mean titer. |   |
| Comparison groups  | MenACWY-CRM Vaccine v Meningococcal Naïve     |
| Number of subjects included in analysis                                      | 99  |
| Analysis specification   | Pre-specified                                 |
| Analysis type  | other   |
| Method   | ANOVA   |
| Parameter estimate   | Vaccine Group Ratios                          |
| Point estimate   | 2.77  |
| Confidence interval  |   |
| level  | 95 %  |
| sides  | 2-sided                                       |
| lower limit  | 1.38  |
| upper limit  | 5.57  |

|  |   |
|--|---|
| <b>Statistical analysis title</b>                              | Statistical Analysis 22 for GMT After Booster                       |
| Statistical analysis description:                              |   |
| Day 8, Men W-135, Pairwise comparison of geometric mean titer. |   |
| Comparison groups  | Meningococcal Naïve v Licensed Polysaccharide Meningococcal Vaccine |
| Number of subjects included in analysis                        | 99  |
| Analysis specification   | Pre-specified   |
| Analysis type  | other   |
| Method   | ANOVA   |
| Parameter estimate   | Vaccine Group Ratios  |
| Point estimate   | 0.54  |
| Confidence interval  |   |
| level  | 95 %  |
| sides  | 2-sided   |
| lower limit  | 0.28  |
| upper limit  | 1.04  |

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Statistical Analysis 23 for GMT After Booster                       |
| Statistical analysis description:<br>Day 8, Men W-135, Pairwise comparison of geometric mean titer. |   |
| Comparison groups   | Licensed Polysaccharide Meningococcal Vaccine v MenACWY-CRM Vaccine |
| Number of subjects included in analysis   | 98  |
| Analysis specification  | Pre-specified   |
| Analysis type   | other   |
| Method  | ANOVA   |
| Parameter estimate  | Vaccine Group Ratios  |
| Point estimate  | 50  |
| Confidence interval   |   |
| level   | 95 %  |
| sides   | 2-sided   |
| lower limit   | 26  |
| upper limit   | 94  |

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Statistical Analysis 24 for GMT After Booster |
| Statistical analysis description:<br>Day 8, Men W-135, Pairwise comparison of geometric mean titer. |   |
| Comparison groups   | MenACWY-CRM Vaccine v Meningococcal Naïve     |
| Number of subjects included in analysis   | 99  |
| Analysis specification  | Pre-specified                                 |
| Analysis type   | other   |
| Method  | ANOVA   |
| Parameter estimate  | Vaccine Group Ratios                          |
| Point estimate  | 27  |
| Confidence interval   |   |
| level   | 95 %  |
| sides   | 2-sided                                       |
| lower limit   | 14  |
| upper limit   | 52  |

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Statistical Analysis 25 for GMT After Booster                       |
| Statistical analysis description:<br>Day 29, Men W-135, Pairwise comparison of geometric mean titer. |   |
| Comparison groups  | Meningococcal Naïve v Licensed Polysaccharide Meningococcal Vaccine |

|   |                      |
|---|----------------------|
| Number of subjects included in analysis | 99                   |
| Analysis specification                  | Pre-specified        |
| Analysis type                           | other                |
| Method                                  | ANOVA                |
| Parameter estimate                      | Vaccine Group Ratios |
| Point estimate                          | 0.6                  |
| Confidence interval                     |                      |
| level                                   | 95 %                 |
| sides                                   | 2-sided              |
| lower limit                             | 0.34                 |
| upper limit                             | 1.04                 |

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Statistical Analysis 26 for GMT After Booster                       |
| Statistical analysis description:<br>Day 29, Men W-135, Pairwise comparison of geometric mean titer. |   |
| Comparison groups  | Licensed Polysaccharide Meningococcal Vaccine v MenACWY-CRM Vaccine |
| Number of subjects included in analysis  | 98  |
| Analysis specification   | Pre-specified   |
| Analysis type  | other   |
| Method   | ANOVA   |
| Parameter estimate   | Vaccine Group Ratios  |
| Point estimate   | 35  |
| Confidence interval  |   |
| level  | 95 %  |
| sides  | 2-sided   |
| lower limit  | 20  |
| upper limit  | 60  |

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Statistical Analysis 27 for GMT After Booster |
| Statistical analysis description:<br>Day 29, Men W-135, Pairwise comparison of geometric mean titer. |   |
| Comparison groups  | MenACWY-CRM Vaccine v Meningococcal Naïve     |
| Number of subjects included in analysis  | 99  |
| Analysis specification   | Pre-specified                                 |
| Analysis type  | other   |
| Method   | ANOVA   |
| Parameter estimate   | Vaccine Group Ratios                          |
| Point estimate   | 21  |
| Confidence interval  |   |
| level  | 95 %  |
| sides  | 2-sided                                       |
| lower limit  | 12  |
| upper limit  | 36  |

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Statistical Analysis 28 for GMT After Booster                       |
| Statistical analysis description:<br>Day 1 (Pre-booster), Men Y, Pairwise comparison of geometric mean titer. |   |
| Comparison groups   | Meningococcal Naïve v Licensed Polysaccharide Meningococcal Vaccine |
| Number of subjects included in analysis   | 99  |
| Analysis specification  | Pre-specified   |
| Analysis type   | other   |
| Method  | ANOVA   |
| Parameter estimate  | Vaccine Group Ratios  |
| Point estimate  | 0.9   |
| Confidence interval   |   |
| level   | 95 %  |
| sides   | 2-sided   |
| lower limit   | 0.48  |
| upper limit   | 1.69  |

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Statistical Analysis 29 for GMT After Booster                       |
| Statistical analysis description:<br>Day 1 (Pre-booster), Men Y, Pairwise comparison of geometric mean titer. |   |
| Comparison groups   | Licensed Polysaccharide Meningococcal Vaccine v MenACWY-CRM Vaccine |
| Number of subjects included in analysis   | 98  |
| Analysis specification  | Pre-specified   |
| Analysis type   | other   |
| Method  | ANOVA   |
| Parameter estimate  | Vaccine Group Ratios  |
| Point estimate  | 3.61  |
| Confidence interval   |   |
| level   | 95 %  |
| sides   | 2-sided   |
| lower limit   | 1.94  |
| upper limit   | 6.74  |

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Statistical Analysis 30 for GMT After Booster |
| Statistical analysis description:<br>Day 1 (Pre-booster), Men Y, Pairwise comparison of geometric mean titer. |   |
| Comparison groups   | MenACWY-CRM Vaccine v Meningococcal Naïve     |

|   |                      |
|---|----------------------|
| Number of subjects included in analysis | 99                   |
| Analysis specification                  | Pre-specified        |
| Analysis type                           | other                |
| Method                                  | ANOVA                |
| Parameter estimate                      | Vaccine Group Ratios |
| Point estimate                          | 3.24                 |
| Confidence interval                     |                      |
| level                                   | 95 %                 |
| sides                                   | 2-sided              |
| lower limit                             | 1.71                 |
| upper limit                             | 6.13                 |

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Statistical Analysis 31 for GMT After Booster                       |
| Statistical analysis description:<br>Day 8, Men Y, Pairwise comparison of geometric mean titer. |   |
| Comparison groups   | Meningococcal Naïve v Licensed Polysaccharide Meningococcal Vaccine |
| Number of subjects included in analysis   | 99  |
| Analysis specification  | Pre-specified   |
| Analysis type   | other   |
| Method  | ANOVA   |
| Parameter estimate  | Vaccine Group Ratios  |
| Point estimate  | 0.33  |
| Confidence interval   |   |
| level   | 95 %  |
| sides   | 2-sided   |
| lower limit   | 0.16  |
| upper limit   | 0.66  |

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Statistical Analysis 32 for GMT After Booster                       |
| Statistical analysis description:<br>Day 8, Men Y, Pairwise comparison of geometric mean titer. |   |
| Comparison groups   | Licensed Polysaccharide Meningococcal Vaccine v MenACWY-CRM Vaccine |
| Number of subjects included in analysis   | 98  |
| Analysis specification  | Pre-specified   |
| Analysis type   | other   |
| Method  | ANOVA   |
| Parameter estimate  | Vaccine Group Ratios  |
| Point estimate  | 121   |
| Confidence interval   |   |
| level   | 95 %  |
| sides   | 2-sided   |
| lower limit   | 61  |
| upper limit   | 241   |

|   |   |
|---|---|
| <b>Statistical analysis title</b>   | Statistical Analysis 33 for GMT After Booster |
| Statistical analysis description:<br>Day 8, Men Y, Pairwise comparison of geometric mean titer. |   |
| Comparison groups   | MenACWY-CRM Vaccine v Meningococcal Naïve     |
| Number of subjects included in analysis   | 99  |
| Analysis specification  | Pre-specified                                 |
| Analysis type   | other   |
| Method  | ANOVA   |
| Parameter estimate  | Vaccine Group Ratios                          |
| Point estimate  | 40  |
| Confidence interval   |   |
| level   | 95 %  |
| sides   | 2-sided                                       |
| lower limit   | 20  |
| upper limit   | 80  |

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Statistical Analysis 34 for GMT After Booster                       |
| Statistical analysis description:<br>Day 29, Men Y, Pairwise comparison of geometric mean titer. |   |
| Comparison groups  | Meningococcal Naïve v Licensed Polysaccharide Meningococcal Vaccine |
| Number of subjects included in analysis  | 99  |
| Analysis specification   | Pre-specified   |
| Analysis type  | other   |
| Method   | ANOVA   |
| Parameter estimate   | Vaccine Group Ratios  |
| Point estimate   | 0.58  |
| Confidence interval  |   |
| level  | 95 %  |
| sides  | 2-sided   |
| lower limit  | 0.32  |
| upper limit  | 1.05  |

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Statistical Analysis 35 for GMT After Booster                       |
| Statistical analysis description:<br>Day 29, Men Y, Pairwise comparison of geometric mean titer. |   |
| Comparison groups  | MenACWY-CRM Vaccine v Licensed Polysaccharide Meningococcal Vaccine |



|   |                      |
|---|----------------------|
| Number of subjects included in analysis | 98                   |
| Analysis specification                  | Pre-specified        |
| Analysis type                           | other                |
| Method                                  | ANOVA                |
| Parameter estimate                      | Vaccine Group Ratios |
| Point estimate                          | 33                   |
| Confidence interval                     |                      |
| level                                   | 95 %                 |
| sides                                   | 2-sided              |
| lower limit                             | 18                   |
| upper limit                             | 60                   |

|  |   |
|--|---|
| <b>Statistical analysis title</b>  | Statistical Analysis 36 for GMT After Booster |
| Statistical analysis description:<br>Day 29, Men Y, Pairwise comparison of geometric mean titer. |   |
| Comparison groups  | MenACWY-CRM Vaccine v Meningococcal Naïve     |
| Number of subjects included in analysis  | 99  |
| Analysis specification   | Pre-specified                                 |
| Analysis type  | other   |
| Method   | ANOVA   |
| Parameter estimate   | Vaccine Group Ratios                          |
| Point estimate   | 19  |
| Confidence interval  |   |
| level  | 95 %  |
| sides  | 2-sided                                       |
| lower limit  | 10  |
| upper limit  | 35  |

### **Secondary: 3. Percentages of Subjects With Serum Bactericidal Activity $\geq 4$ at 5 Years After Primary Vaccination**

|   |   |
|---|---|
| End point title   | 3. Percentages of Subjects With Serum Bactericidal Activity $\geq 4$ at 5 Years After Primary Vaccination |
| End point description:<br>Persistence was measured by percentages of subjects with hSBA $\geq 4$ in previously vaccinated subjects and in age-matched meningococcal vaccine naïve subjects. Sera was tested against N. Meningitidis serogroups A, C, W-135 and Y.<br>The analysis was done on the FAS, Antibody Persistence (FAS Persist) Population. |   |
| End point type  | Secondary   |
| End point timeframe:<br>Day 1 (5 years after primary vaccination).  |   |

| End point values                 | MenACWY-CRM Vaccine | Licensed Polysaccharide Meningococcal Vaccine | Meningococcal Naïve |  |
|----------------------------------|---------------------|---|---------------------|--|
| Subject group type               | Reporting group     | Reporting group                               | Reporting group     |  |
| Number of subjects analysed      | 50                  | 50  | 53                  |  |
| Units: Percentages of Subjects   |                     |   |                     |  |
| number (confidence interval 95%) |                     |   |                     |  |
| Men A                            | 34 (21 to 49)       | 50 (36 to 64)                                 | 23 (12 to 36)       |  |
| Men C                            | 84 (71 to 93)       | 68 (53 to 80)                                 | 70 (56 to 82)       |  |
| Men W-135                        | 80 (66 to 90)       | 58 (43 to 72)                                 | 55 (40 to 68)       |  |
| Men Y                            | 76 (62 to 87)       | 60 (45 to 74)                                 | 60 (46 to 74)       |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: 4. Geometric Mean Titer at 5 Years After Primary Vaccination

|   |  |
|---|--|
| End point title   | 4. Geometric Mean Titer at 5 Years After Primary Vaccination |
| End point description:  |  |
| Persistence was measured by hSBA and expressed as hSBA GMT in previously vaccinated subjects and in age-matched meningococcal vaccine naïve subjects. Sera were tested against Neisseria meningitidis serogroups A, C, W-135 and Y. |  |
| The analysis was done on the FAS, Antibody Persistence (FAS Persist) Population.  |  |
| End point type  | Secondary  |
| End point timeframe:  |  |
| Day 1 (5 years after primary vaccination).  |  |

| End point values                         | MenACWY-CRM Vaccine | Licensed Polysaccharide Meningococcal Vaccine | Meningococcal Naïve |  |
|--|---------------------|---|---------------------|--|
| Subject group type                       | Reporting group     | Reporting group                               | Reporting group     |  |
| Number of subjects analysed              | 50                  | 50  | 53                  |  |
| Units: Titers                            |                     |   |                     |  |
| geometric mean (confidence interval 95%) |                     |   |                     |  |
| Men A                                    | 5.21 (3.51 to 7.74) | 7.56 (5.12 to 11)                             | 3 (2.05 to 4.4)     |  |
| Men C                                    | 20 (12 to 31)       | 19 (12 to 30)                                 | 7.62 (4.86 to 12)   |  |
| Men W-135                                | 28 (17 to 46)       | 12 (7.17 to 20)                               | 11 (6.53 to 17)     |  |
| Men Y                                    | 27 (17 to 43)       | 7.67 (4.85 to 12)                             | 9.38 (5.98 to 15)   |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: 5. Percentages of Subjects With Serum Bactericidal Activity $\geq 4$ After Booster Vaccination

|                 |  |
|-----------------|--|
| End point title | 5. Percentages of Subjects With Serum Bactericidal Activity $\geq 4$ After Booster Vaccination |
|-----------------|--|

End point description:

Immunogenicity was measured by hSBA  $\geq 4$  in previously vaccinated subjects and in age-matched meningococcal vaccine naïve subjects. Sera were tested against *Neisseria meningitidis* serogroups A, C, W-135 and Y.

The analysis was done on the FAS, Immunogenicity after one dose of MenACWY (FAS Booster) Population.

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

End point timeframe:

Day 7, Day 28 post booster (5 years after primary vaccination).

| End point values                 | MenACWY-CRM Vaccine | Licensed Polysaccharide Meningococcal Vaccine | Meningococcal Naïve |  |
|----------------------------------|---------------------|---|---------------------|--|
| Subject group type               | Reporting group     | Reporting group                               | Reporting group     |  |
| Number of subjects analysed      | 49                  | 49  | 50                  |  |
| Units: Percentages of Subjects   |                     |   |                     |  |
| number (confidence interval 95%) |                     |   |                     |  |
| Day 7 post booster , Men A       | 100 (93 to 100)     | 76 (61 to 87)                                 | 66 (51 to 79)       |  |
| Day 28 post booster, Men A       | 98 (89 to 100)      | 94 (83 to 99)                                 | 92 (81 to 98)       |  |
| Day 7 post booster, Men C        | 100 (93 to 100)     | 82 (68 to 91)                                 | 94 (83 to 99)       |  |
| Day 28 post booster, Men C       | 100 (93 to 100)     | 90 (78 to 97)                                 | 98 (89 to 100)      |  |
| Day 7 post booster, Men W-135    | 100 (93 to 100)     | 86 (73 to 94)                                 | 92 (81 to 98)       |  |
| Day 28 post booster, Men W-135   | 100 (93 to 100)     | 94 (83 to 99)                                 | 94 (83 to 99)       |  |
| Day 7 post booster, Men Y        | 98 (89 to 100)      | 78 (63 to 88)                                 | 92 (81 to 98)       |  |
| Day 28 post booster, Men Y       | 100 (93 to 100)     | 100 (93 to 100)                               | 100 (93 to 100)     |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: 6. Percentages of Subjects With Serum Bactericidal Activity $\geq 8$ After Booster Vaccination

|                 |  |
|-----------------|--|
| End point title | 6. Percentages of Subjects With Serum Bactericidal Activity $\geq 8$ After Booster Vaccination |
|-----------------|--|

End point description:

Immunogenicity was measured by serum bactericidal assay with human complement (hSBA)  $\geq 8$  in previously vaccinated subjects and in age-matched meningococcal vaccine naïve subjects. Sera were tested against *Neisseria meningitidis* serogroups A, C, W-135 and Y.

The analysis was done on the FAS, Immunogenicity after one dose of MenACWY (FAS Booster)

Population.

|   |           |
|---|-----------|
| End point type  | Secondary |
| End point timeframe:  |           |
| Day 7, Day 28 post booster (5 years after primary vaccination). |           |

| End point values                 | MenACWY-CRM Vaccine | Licensed Polysaccharide Meningococcal Vaccine | Meningococcal Naïve |  |
|----------------------------------|---------------------|---|---------------------|--|
| Subject group type               | Reporting group     | Reporting group                               | Reporting group     |  |
| Number of subjects analysed      | 49                  | 49  | 50                  |  |
| Units: Percentages of Subjects   |                     |   |                     |  |
| number (confidence interval 95%) |                     |   |                     |  |
| Day 7 post booster, Men A        | 100 (93 to 100)     | 73 (59 to 85)                                 | 64 (49 to 77)       |  |
| Day 28 post booster, Men A       | 98 (89 to 100)      | 94 (83 to 99)                                 | 92 (81 to 98)       |  |
| Day 7 post booster, Men C        | 100 (93 to 100)     | 78 (63 to 88)                                 | 90 (78 to 97)       |  |
| Day 28 post booster, Men C       | 100 (93 to 100)     | 84 (70 to 93)                                 | 98 (89 to 100)      |  |
| Day 7 post booster, Men W-135    | 100 (93 to 100)     | 84 (70 to 93)                                 | 88 (76 to 95)       |  |
| Day 28 post booster, Men W-135   | 100 (93 to 100)     | 92 (80 to 98)                                 | 94 (83 to 99)       |  |
| Day 7 post booster, Men Y        | 98 (89 to 100)      | 76 (61 to 87)                                 | 90 (78 to 97)       |  |
| Day 28 post booster, Men Y       | 100 (93 to 100)     | 96 (86 to 100)                                | 98 (89 to 100)      |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: 7. Geometric Mean Ratio After Booster Vaccination

|   |   |
|---|---|
| End point title   | 7. Geometric Mean Ratio After Booster Vaccination |
| End point description:  |   |
| Ratios are expressed as geometric mean titer at Day 8: Day 1 and at Day 29:Day 1.<br>The analysis was done on the FAS, Immunogenicity after one dose of MenACWY (FAS Booster) Population. |   |
| End point type  | Secondary   |
| End point timeframe:  |   |
| Day 8 and Day 29 (at 5 Years After Primary Vaccination).  |   |

| End point values                         | MenACWY-CRM Vaccine | Licensed Polysaccharide Meningococcal Vaccine | Meningococcal Naïve |  |
|--|---------------------|---|---------------------|--|
| Subject group type                       | Reporting group     | Reporting group                               | Reporting group     |  |
| Number of subjects analysed              | 49                  | 49  | 50                  |  |
| Units: Ratios                            |                     |   |                     |  |
| geometric mean (confidence interval 95%) |                     |   |                     |  |
| Men A (Day 8:1)                          | 205 (113 to 373)    | 6.1 (3.4 to 11)                               | 11 (6.17 to 20)     |  |
| Men A (Day 29:1), N=48, N=49, N=50       | 155 (92 to 262)     | 20 (12 to 33)                                 | 37 (22 to 62)       |  |
| Men C (Day 8:1)                          | 78 (47 to 130)      | 1.85 (1.13 to 3.03)                           | 9.48 (5.76 to 16)   |  |
| Men C (Day 29:1)                         | 60 (37 to 97)       | 2.64 (1.64 to 4.24)                           | 17 (11 to 28)       |  |
| Men W-135 (Day 8:1)                      | 58 (34 to 97)       | 2.92 (1.75 to 4.87)                           | 5.95 (3.55 to 9.99) |  |
| Men W-135 (Day 29:1)                     | 56 (33 to 95)       | 4.06 (2.43 to 6.077)                          | 7.48 (4.46 to 13)   |  |
| Men Y (Day 8:1), N=48, N=49, N=50        | 96 (56 to 167)      | 2.69 (1.58 to 4.58)                           | 7.29 (4.26 to 12)   |  |
| Men Y (Day 29:1)                         | 74 (43 to 129)      | 8.12 (4.73 to 14)                             | 13 (7.3 to 22)      |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: 8. Percentages of Subjects With hSBA Seroresponse After Booster Vaccination

|   |   |
|---|---|
| End point title   | 8. Percentages of Subjects With hSBA Seroresponse After Booster Vaccination |
| End point description:<br>For a subject with hSBA titer <4 at baseline, seroresponse is defined as a post-vaccination hSBA titer ≥8; and for a subject with hSBA titer ≥4 at baseline, seroresponse is defined as a post-vaccination hSBA titer of at least 4 times the baseline. Sera were tested against Neisseria meningitidis serogroups A, C, W-135 and Y.<br>The analysis was done on the FAS, Immunogenicity after one dose of MenACWY (FAS Booster) Population. |   |
| End point type  | Secondary   |
| End point timeframe:<br>Day 8, Day 29 (5 years after primary vaccination).  |   |

| End point values                 | MenACWY-CRM Vaccine | Licensed Polysaccharide Meningococcal Vaccine | Meningococcal Naïve |  |
|----------------------------------|---------------------|---|---------------------|--|
| Subject group type               | Reporting group     | Reporting group                               | Reporting group     |  |
| Number of subjects analysed      | 49                  | 49  | 50                  |  |
| Units: Percentages of Subjects   |                     |   |                     |  |
| number (confidence interval 95%) |                     |   |                     |  |

|                   |                 |               |               |  |
|-------------------|-----------------|---------------|---------------|--|
| Men A, Day 8      | 100 (93 to 100) | 51 (36 to 66) | 60 (45 to 74) |  |
| Men A, Day 29     | 100 (93 to 100) | 76 (61 to 87) | 90 (78 to 97) |  |
| Men C, Day 8      | 96 (86 to 100)  | 16 (7 to 30)  | 62 (47 to 75) |  |
| Men C, Day 29     | 96 (86 to 100)  | 31 (18 to 45) | 80 (66 to 90) |  |
| Men W-135, Day 8  | 96 (86 to 100)  | 37 (23 to 52) | 48 (34 to 63) |  |
| Men W-135, Day 29 | 98 (89 to 100)  | 47 (33 to 62) | 58 (43 to 72) |  |
| Men Y, Day 8      | 94 (83 to 99)   | 33 (20 to 48) | 54 (39 to 68) |  |
| Men Y, Day 29     | 94 (83 to 99)   | 55 (40 to 69) | 76 (62 to 87) |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: 9. Number of Subjects With at Least One Reactogenicity Sign After Booster Vaccination

|   |   |
|---|---|
| End point title   | 9. Number of Subjects With at Least One Reactogenicity Sign After Booster Vaccination |
| End point description:  |   |
| Local and systemic reactions were solicited to assess safety and tolerability of vaccination. The analysis was done on the safety population. |   |
| End point type  | Secondary   |
| End point timeframe:  |   |
| Up to Day 7.  |   |

| End point values                | MenACWY-CRM Vaccine | Licensed Polysaccharide Meningococcal Vaccine | Meningococcal Naïve |  |
|---------------------------------|---------------------|---|---------------------|--|
| Subject group type              | Reporting group     | Reporting group                               | Reporting group     |  |
| Number of subjects analysed     | 50                  | 50  | 53                  |  |
| Units: Number of Subjects       |                     |   |                     |  |
| number (not applicable)         |                     |   |                     |  |
| Local Reactions (any-total)     | 30                  | 32  | 40                  |  |
| Pain (any)                      | 29                  | 27  | 33                  |  |
| Erythema (any)                  | 8                   | 8   | 15                  |  |
| Induration (any)                | 5                   | 8   | 5                   |  |
| Systemic Reactions (any-total)  | 31                  | 25  | 38                  |  |
| Chills (any)                    | 7                   | 5   | 3                   |  |
| Nausea (any)                    | 8                   | 9   | 11                  |  |
| Malaise (any)                   | 10                  | 11  | 15                  |  |
| Myalgia (any)                   | 16                  | 13  | 17                  |  |
| Arthralgia (any)                | 3                   | 5   | 6                   |  |
| Headache (any)                  | 21                  | 17  | 31                  |  |
| Fever ( ≥ 38C ) (any)           | 0                   | 0   | 1                   |  |
| Stayed Home (any)               | 0                   | 2   | 2                   |  |
| Analges Antipyr Meds Used (any) | 10                  | 8   | 9                   |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: 10. Number of Subjects With Unsolicited Adverse Events After Booster Vaccination

|                 |  |
|-----------------|--|
| End point title | 10. Number of Subjects With Unsolicited Adverse Events After Booster Vaccination |
|-----------------|--|

End point description:

Number of subjects with unsolicited Adverse Events (AEs) within 7 days (day 1-7) after the vaccination. The analysis was done on the safety population.

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

End point timeframe:

Up to Day 7.

| End point values                    | MenACWY-CRM Vaccine | Licensed Polysaccharide Meningococcal Vaccine | Meningococcal Naïve |  |
|-------------------------------------|---------------------|---|---------------------|--|
| Subject group type                  | Reporting group     | Reporting group                               | Reporting group     |  |
| Number of subjects analysed         | 50                  | 50  | 53                  |  |
| Units: Subjects                     |                     |   |                     |  |
| Any-Adverse Event                   | 12                  | 7   | 10                  |  |
| Ear & Labyrinth Disorders           | 0                   | 0   | 1                   |  |
| Eye Disorders                       | 1                   | 0   | 1                   |  |
| Gastrointestinal Disorders          | 1                   | 1   | 0                   |  |
| Gen. Disorders & Admin. Site Cond.  | 2                   | 3   | 4                   |  |
| Infections & Infestations           | 4                   | 1   | 2                   |  |
| Injury & Poisoning                  | 0                   | 1   | 1                   |  |
| Musculo., Connect. Tis. & Bone Dis. | 4                   | 0   | 2                   |  |
| Nervous System Disorders            | 4                   | 2   | 4                   |  |
| Resp., Thoracic & Mediastinal Dis.  | 0                   | 1   | 0                   |  |
| Skin & Subcutaneous Tis. Disorders  | 2                   | 0   | 0                   |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Safety was assessed up to 28 days after vaccination.

Adverse event reporting additional description:

All the AEs reported were solicited post-injection reactions.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 17.1 |
|--------------------|------|

### Reporting groups

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

Reporting group description:

Subjects had been given one dose of Meningococcal ACWY (MenACWY) vaccine conjugated to CRM197 (cross-reactive material-mutant of diphtheria toxin) 5 years ago.

|                       |                     |
|-----------------------|---------------------|
| Reporting group title | Meningococcal Naïve |
|-----------------------|---------------------|

Reporting group description:

Subjects were between 16 years to 23 years (age-inclusive) and meningococcal vaccine naïve.

|                       |   |
|-----------------------|---|
| Reporting group title | Licensed Polysaccharide Meningococcal Vaccine |
|-----------------------|---|

Reporting group description:

Subjects had been given one dose of licensed Meningococcal (Men ACWY) polysaccharide vaccine (Menomune®) 5 years ago.

| Serious adverse events                            | MenACWY-CRM Vaccine | Meningococcal Naïve | Licensed Polysaccharide Meningococcal Vaccine |
|---|---------------------|---------------------|---|
| Total subjects affected by serious adverse events |                     |                     |   |
| subjects affected / exposed                       | 0 / 50 (0.00%)      | 0 / 53 (0.00%)      | 0 / 50 (0.00%)                                |
| number of deaths (all causes)                     | 0                   | 0                   | 0   |
| number of deaths resulting from adverse events    | 0                   | 0                   | 0   |

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

| Non-serious adverse events                            | MenACWY-CRM Vaccine | Meningococcal Naïve | Licensed Polysaccharide Meningococcal Vaccine |
|---|---------------------|---------------------|---|
| Total subjects affected by non-serious adverse events |                     |                     |   |
| subjects affected / exposed                           | 38 / 50 (76.00%)    | 46 / 53 (86.79%)    | 36 / 50 (72.00%)                              |
| Nervous system disorders                              |                     |                     |   |
| Headache  |                     |                     |   |



|   |                        |                        |                        |
|---|------------------------|------------------------|------------------------|
| subjects affected / exposed<br>occurrences (all)        | 21 / 50 (42.00%)<br>26 | 31 / 53 (58.49%)<br>43 | 17 / 50 (34.00%)<br>24 |
| General disorders and administration<br>site conditions |                        |                        |                        |
| Chills  |                        |                        |                        |
| subjects affected / exposed                             | 7 / 50 (14.00%)        | 3 / 53 (5.66%)         | 5 / 50 (10.00%)        |
| occurrences (all)                                       | 8                      | 4                      | 6                      |
| Injection site erythema                                 |                        |                        |                        |
| subjects affected / exposed                             | 8 / 50 (16.00%)        | 15 / 53 (28.30%)       | 8 / 50 (16.00%)        |
| occurrences (all)                                       | 8                      | 15                     | 9                      |
| Injection site induration                               |                        |                        |                        |
| subjects affected / exposed                             | 5 / 50 (10.00%)        | 5 / 53 (9.43%)         | 8 / 50 (16.00%)        |
| occurrences (all)                                       | 5                      | 5                      | 8                      |
| Injection site pain                                     |                        |                        |                        |
| subjects affected / exposed                             | 29 / 50 (58.00%)       | 33 / 53 (62.26%)       | 27 / 50 (54.00%)       |
| occurrences (all)                                       | 31                     | 39                     | 28                     |
| Malaise   |                        |                        |                        |
| subjects affected / exposed                             | 10 / 50 (20.00%)       | 15 / 53 (28.30%)       | 11 / 50 (22.00%)       |
| occurrences (all)                                       | 12                     | 18                     | 12                     |
| Gastrointestinal disorders                              |                        |                        |                        |
| Nausea  |                        |                        |                        |
| subjects affected / exposed                             | 8 / 50 (16.00%)        | 11 / 53 (20.75%)       | 9 / 50 (18.00%)        |
| occurrences (all)                                       | 8                      | 15                     | 10                     |
| Musculoskeletal and connective tissue<br>disorders      |                        |                        |                        |
| Arthralgia  |                        |                        |                        |
| subjects affected / exposed                             | 3 / 50 (6.00%)         | 6 / 53 (11.32%)        | 5 / 50 (10.00%)        |
| occurrences (all)                                       | 4                      | 6                      | 6                      |
| Myalgia   |                        |                        |                        |
| subjects affected / exposed                             | 18 / 50 (36.00%)       | 18 / 53 (33.96%)       | 13 / 50 (26.00%)       |
| occurrences (all)                                       | 21                     | 25                     | 13                     |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date            | Amendment  |
|-----------------|--|
| 19 January 2010 | Update of some analysis collection, physical assessment and study visits procedures. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

|     |
|-----|
| N/A |
|-----|

Notes:

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### Online references

<http://www.ncbi.nlm.nih.gov/pubmed/23114372>