



## Clinical trial results:

**A Phase IIIb, Open Label, Controlled, Multi-Center Study to Evaluate the Safety, Tolerability and Immunogenicity of Two Doses of Novartis Meningococcal Group B Vaccine when administered to Immunocompromised Patients from 2 to 17 years of age who are at Increased Risk of Meningococcal Disease because of Complement Deficiency or Asplenia compared to matched Healthy Controls.**

### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2013-002454-78  |
| Trial protocol           | IT ES PL        |
| Global end of trial date | 22 October 2015 |

### Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v1 (current)  |
| This version publication date  | 19 March 2016 |
| First version publication date | 19 March 2016 |

### Trial information

#### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | V72_62 |
|-----------------------|--------|

#### Additional study identifiers

|                                    |                                |
|------------------------------------|--------------------------------|
| ISRCTN number                      | -                              |
| ClinicalTrials.gov id (NCT number) | NCT02141516                    |
| WHO universal trial number (UTN)   | -                              |
| Other trial identifiers            | Not applicable: Not applicable |

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)       | Yes                 |
| EMA paediatric investigation plan number(s)                          | EMA-000139-PIP01-07 |
| 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                       | 15 February 2016 |
| Is this the analysis of the primary completion data? | Yes              |
| Primary completion date                              | 16 March 2015    |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 22 October 2015  |
| Was the trial ended prematurely?                     | No               |

Notes:

## General information about the trial

Main objective of the trial:

Immunogenicity Objective

- To evaluate the immunogenicity of two doses of rMenB+OMV NZ in subjects with increased risk of meningococcal disease because of complement deficiency or asplenia and in healthy age-matched subjects, at 1 month after the second vaccination.

Safety Objective

- To assess the safety and tolerability of two doses of rMenB+OMV NZ in subjects with increased risk of meningococcal disease because of complement deficiency or asplenia and in healthy age-matched subjects.

Protection of trial subjects:

This clinical study was designed and shall be implemented and reported in accordance with the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Harmonized Tripartite Guidelines for Good Clinical Practice (GCP), with applicable local regulations: including European Directive 2001/20/EC, Novartis codes on protection of human rights, and with the ethical principles laid down in the Declaration of Helsinki (European Council 2001, US Code of Federal Regulations, ICH 1997).

Background therapy: -

Evidence for comparator: -

|   |             |
|---|-------------|
| Actual start date of recruitment                          | 27 May 2014 |
| 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 | Russian Federation: 45 |
| Country: Number of subjects enrolled | Poland: 57             |
| Country: Number of subjects enrolled | Spain: 66              |
| Country: Number of subjects enrolled | United Kingdom: 38     |
| Country: Number of subjects enrolled | Italy: 33              |
| Worldwide total number of subjects   | 239                    |
| EEA total number of subjects         | 194                    |

Notes:

| <b>Subjects enrolled per age group</b>    |     |
|---|-----|
| 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)                     | 132 |
| Adolescents (12-17 years)                 | 107 |
| Adults (18-64 years)                      | 0   |
| From 65 to 84 years                       | 0   |
| 85 years and over                         | 0   |

## Subject disposition

### Recruitment

Recruitment details:

Subjects were enrolled at 4 centers in Italy, 3 centers in Poland, 3 centers in the Russian Federation, 4 centers in Spain and 4 centers in the United Kingdom.

### Pre-assignment

Screening details:

All the enrolled subjects were included in the trial.

### Period 1

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

Blinding implementation details:

The trial is designed as an open-label study and all subjects will receive the same treatment.

### Arms

|                              |         |
|------------------------------|---------|
| Are arms mutually exclusive? | No      |
| <b>Arm title</b>             | CompDef |

Arm description:

Subjects aged  $\geq 2$  to  $\leq 17$  years with complement deficiencies received 2 doses of rMenB+OMV NZ administered 2 months apart.

|  |  |
|--|--|
| Arm type                               | Experimental                               |
| Investigational medicinal product name | Meningococcal (group B)                    |
| Investigational medicinal product code |  |
| Other name                             | rMenB+OMV NZ                               |
| Pharmaceutical forms                   | Suspension for injection in pre-filled pen |
| Routes of administration               | Intramuscular use                          |

Dosage and administration details:

Two doses of 0.5 mL each administered 2 months apart.

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

Arm description:

Subjects aged  $\geq 2$  to  $\leq 17$  years with Asplenia received 2 doses of rMenB+OMV NZ administered 2 months apart.

|  |  |
|--|--|
| Arm type                               | Experimental                               |
| Investigational medicinal product name | Meningococcal (group B)                    |
| Investigational medicinal product code |  |
| Other name                             | rMenB+OMV NZ                               |
| Pharmaceutical forms                   | Suspension for injection in pre-filled pen |
| Routes of administration               | Intramuscular use                          |

Dosage and administration details:

Two doses of 0.5 mL each administered 2 months apart.

|                  |                  |
|------------------|------------------|
| <b>Arm title</b> | CompDef+Asplenia |
|------------------|------------------|

Arm description:

Subjects aged  $\geq 2$  to  $\leq 17$  years with either complement deficiencies or Asplenia received 2 doses of rMenB+OMV NZ administered 2 months apart.

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

|   |  |
|---|--|
| Investigational medicinal product name  | Meningococcal (group B)                    |
| Investigational medicinal product code  |  |
| Other name  | rMenB+OMV NZ                               |
| Pharmaceutical forms  | Suspension for injection in pre-filled pen |
| Routes of administration  | Intramuscular use                          |
| Dosage and administration details:<br>Two doses of 0.5 mL each administered 2 months apart. |  |
| <b>Arm title</b>  | Healthy Subjects                           |

Arm description:

Healthy subjects aged  $\geq 2$  to  $\leq 17$  years received 2 doses of rMenB+OMV NZ administered 2 months apart.

|  |  |
|--|--|
| Arm type                               | Experimental                               |
| Investigational medicinal product name | Meningococcal (group B)                    |
| Investigational medicinal product code |  |
| Other name                             | rMenB+OMV NZ                               |
| Pharmaceutical forms                   | Suspension for injection in pre-filled pen |
| Routes of administration               | Intramuscular use                          |

Dosage and administration details:

Two doses of 0.5 mL each administered 2 months apart.

| <b>Number of subjects in period 1</b> | CompDef | Asplenia | CompDef+Asplenia |
|---------------------------------------|---------|----------|------------------|
| Started                               | 40      | 112      | 152              |
| Completed                             | 40      | 107      | 147              |
| Not completed                         | 0       | 5        | 5                |
| Adverse event, non-fatal              | -       | 1        | 1                |
| Other                                 | -       | 3        | 3                |
| Lost to follow-up                     | -       | 1        | 1                |

| <b>Number of subjects in period 1</b> | Healthy Subjects |
|---------------------------------------|------------------|
| Started                               | 87               |
| Completed                             | 87               |
| Not completed                         | 0                |
| Adverse event, non-fatal              | -                |
| Other                                 | -                |
| Lost to follow-up                     | -                |

## Baseline characteristics

### Reporting groups

|   |                  |
|---|------------------|
| Reporting group title   | CompDef          |
| Reporting group description:<br>Subjects aged $\geq 2$ to $\leq 17$ years with complement deficiencies received 2 doses of rMenB+OMV NZ administered 2 months apart.                    |                  |
| Reporting group title   | Asplenia         |
| Reporting group description:<br>Subjects aged $\geq 2$ to $\leq 17$ years with Asplenia received 2 doses of rMenB+OMV NZ administered 2 months apart.                                   |                  |
| Reporting group title   | CompDef+Asplenia |
| Reporting group description:<br>Subjects aged $\geq 2$ to $\leq 17$ years with either complement deficiencies or Asplenia received 2 doses of rMenB+OMV NZ administered 2 months apart. |                  |
| Reporting group title   | Healthy Subjects |
| Reporting group description:<br>Healthy subjects aged $\geq 2$ to $\leq 17$ years received 2 doses of rMenB+OMV NZ administered 2 months apart.   |                  |

| Reporting group values                             | CompDef    | Asplenia  | CompDef+Asplenia |
|--|------------|-----------|------------------|
| Number of subjects                                 | 40         | 112       | 152              |
| Age categorical<br>Units: Subjects                 |            |           |                  |
| In utero   |            |           |                  |
| Preterm newborn infants (gestational age < 37 wks) |            |           |                  |
| Newborns (0-27 days)                               |            |           |                  |
| Infants and toddlers (28 days-23 months)           |            |           |                  |
| Children (2-11 years)                              |            |           |                  |
| Adolescents (12-17 years)                          |            |           |                  |
| Adults (18-64 years)                               |            |           |                  |
| From 65-84 years                                   |            |           |                  |
| 85 years and over                                  |            |           |                  |
| Age continuous<br>Units: years                     |            |           |                  |
| arithmetic mean                                    | 8.5        | 11.1      | 10.4             |
| standard deviation                                 | $\pm 4.35$ | $\pm 3.7$ | $\pm 4.03$       |
| Gender categorical<br>Units: Subjects              |            |           |                  |
| Female   | 17         | 46        | 63               |
| Male   | 23         | 66        | 89               |

| Reporting group values                             | Healthy Subjects | Total |  |
|--|------------------|-------|--|
| Number of subjects                                 | 87               | 239   |  |
| Age categorical<br>Units: Subjects                 |                  |       |  |
| In utero   |                  |       |  |
| Preterm newborn infants (gestational age < 37 wks) |                  |       |  |

|   |                |     |  |
|---|----------------|-----|--|
| 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<br>arithmetic mean<br>standard deviation   | 10.2<br>± 4.14 | -   |  |
| Gender categorical<br>Units: Subjects   |                |     |  |
| Female  | 44             | 107 |  |
| Male  | 43             | 132 |  |

## End points

### End points reporting groups

|  |   |
|--|---|
| Reporting group title  | CompDef                                     |
| Reporting group description:<br>Subjects aged $\geq 2$ to $\leq 17$ years with complement deficiencies received 2 doses of rMenB+OMV NZ administered 2 months apart.   |   |
| Reporting group title  | Asplenia                                    |
| Reporting group description:<br>Subjects aged $\geq 2$ to $\leq 17$ years with Asplenia received 2 doses of rMenB+OMV NZ administered 2 months apart.  |   |
| Reporting group title  | CompDef+Asplenia                            |
| Reporting group description:<br>Subjects aged $\geq 2$ to $\leq 17$ years with either complement deficiencies or Asplenia received 2 doses of rMenB+OMV NZ administered 2 months apart.  |   |
| Reporting group title  | Healthy Subjects                            |
| Reporting group description:<br>Healthy subjects aged $\geq 2$ to $\leq 17$ years received 2 doses of rMenB+OMV NZ administered 2 months apart.  |   |
| Subject analysis set title   | All Enrolled Set                            |
| Subject analysis set type  | Intention-to-treat                          |
| Subject analysis set description:<br>All screened subjects who provide informed consent and provide demographic and/or baseline screening assessments, regardless of the subject's treatment status in the trial and received a subject ID.  |   |
| Subject analysis set title   | Full Analysis Set (FAS), Immunogenicity Set |
| Subject analysis set type  | Full analysis                               |
| Subject analysis set description:<br>All subjects in the Enrolled Population who received a study vaccination and provided an evaluable serum sample at one month after the second dose of rMenB+OMV NZ whose assay result is available for at least one of the serogroup B indicator strains or M10713 strain or Enzyme-linked Immunosorbent Assay (ELISA). |   |
| Subject analysis set title   | Solicited Safety Set                        |
| Subject analysis set type  | Safety analysis                             |
| Subject analysis set description:<br>All subjects in the Exposed Set with any solicited adverse event data.  |   |
| Subject analysis set title   | Unsolicited Safety Set                      |
| Subject analysis set type  | Safety analysis                             |
| Subject analysis set description:<br>All subjects in the Exposed Set with post-vaccination unsolicited adverse event records.  |   |
| Subject analysis set title   | Overall Safety Set                          |
| Subject analysis set type  | Safety analysis                             |
| Subject analysis set description:<br>All subjects in the Exposed Set with any adverse event data.  |   |

### Primary: 1. Percentages of subjects with serum bactericidal activity using human complement (hSBA) titers $\geq 5$ against N. meningitidis serogroup.

|  |   |
|--|---|
| End point title  | 1. Percentages of subjects with serum bactericidal activity using human complement (hSBA) titers $\geq 5$ against N. meningitidis serogroup. <sup>[1]</sup> |
| End point description:<br>Immunogenicity was assessed in terms of percentage of subjects with hSBA titers $\geq 5$ against N. meningitidis serogroup B indicator strains (H44/76, 5/99, and NZ98/254) and M10713 strain following 2 doses of rMenB+OMV NZ, administered on Day 1 and Day 61. The analysis was done on Full Analysis Set (FAS). |   |



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

End point timeframe:

Day 1 and Day 91 (one month after the second dose of the study vaccine).

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 was associated to this endpoint. Analyses were run descriptively.

| End point values                   | CompDef           | Asplenia          | CompDef+Asplenia   | Healthy Subjects   |
|------------------------------------|-------------------|-------------------|--------------------|--------------------|
| Subject group type                 | Reporting group   | Reporting group   | Reporting group    | Reporting group    |
| Number of subjects analysed        | 39                | 106               | 144                | 85                 |
| Units: Percentages of Subjects     |                   |                   |                    |                    |
| number (confidence interval 95%)   |                   |                   |                    |                    |
| H44/76; Day 1 (N=39,104,143,84)    | 0 (0 to 9)        | 7 (2.7 to 13.4)   | 5 (2 to 9.8)       | 6 (2 to 13.3)      |
| H44/76; Day 91 (N=39,104,143,85)   | 87 (72.6 to 95.7) | 97 (91.8 to 99.4) | 94 (89.3 to 97.6)  | 98 (91.8 to 99.71) |
| 5/99; Day 1 (N=37,103,140,82)      | 0 (0 to 9.5)      | 12 (6.2 to 19.5)  | 9 (4.5 to 14.5)    | 6 (2 to 13.7)      |
| 5/99; Day 91 (N=38,106,144,83)     | 95 (82.3 to 99.4) | 100 (96.6 to 100) | 99 (95.1 to 99.83) | 99 (93.5 to 99.97) |
| NZ98/254; Day 1 (N=36,105,141,83)  | 0 (0 to 9.7)      | 4 (1 to 9.5)      | 3 (0.8 to 7.1)     | 2 (0.29 to 8.4)    |
| NZ98/254; Day 91 (N=38,106,144,84) | 68 (51.3 to 82.5) | 86 (77.7 to 91.9) | 81 (73.9 to 87.3)  | 83 (73.6 to 90.6)  |
| M10713; Day 1 (N=36,102,138,82)    | 56 (38.1 to 72.1) | 79 (70.3 to 86.8) | 73 (65 to 80.4)    | 78 (67.5 to 86.4)  |
| M10713; Day 91 (N=37,103,140,83)   | 73 (55.9 to 86.2) | 94 (87.8 to 97.8) | 89 (82.1 to 93.3)  | 99 (93.5 to 99.97) |

## Statistical analyses

No statistical analyses for this end point

### Primary: 2. Percentages of subjects with serum bactericidal activity hSBA titers $\geq 8$ against N. meningitidis serogroup.

|                 |  |
|-----------------|--|
| End point title | 2. Percentages of subjects with serum bactericidal activity hSBA titers $\geq 8$ against N. meningitidis serogroup. <sup>[2]</sup> |
|-----------------|--|

End point description:

Immunogenicity was assessed in terms of percentage of subjects with hSBA titers  $\geq 8$  against N. meningitidis serogroup B indicator strains (H44/76, 5/99, and NZ98/254) and M10713 strain following 2 doses of rMenB+OMV NZ, administered on Day 1 and Day 61. The analysis was done on Full Analysis Set (FAS).

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

End point timeframe:

Day 1 and Day 91 (one month after the second dose of the study vaccine).

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis was associated to this endpoint. Analyses were run descriptively.

| End point values                   | CompDef           | Asplenia          | CompDef+Asplenia  | Healthy Subjects   |
|------------------------------------|-------------------|-------------------|-------------------|--------------------|
| Subject group type                 | Reporting group   | Reporting group   | Reporting group   | Reporting group    |
| Number of subjects analysed        | 39                | 106               | 144               | 85                 |
| Units: Percentages of Subjects     |                   |                   |                   |                    |
| number (confidence interval 95%)   |                   |                   |                   |                    |
| H44/76; Day 1 (N=39,104,143,84)    | 0 (0 to 9)        | 2 (0.23 to 6.8)   | 1 (0.17 to 5)     | 2 (0.29 to 8.3)    |
| H44/76; Day 91 (N=39,104,143,85)   | 87 (72.6 to 95.7) | 95 (89.1 to 98.4) | 93 (87.5 to 96.6) | 98 (91.8 to 99.71) |
| 5/99; Day 1 (N=37,103,140,82)      | 0 (0 to 9.5)      | 11 (5.5 to 18.3)  | 8 (4 to 13.6)     | 5 (1.3 to 12)      |
| 5/99; Day 91 (N=38,106,144,83)     | 92 (78.6 to 98.3) | 100 (96.6 to 100) | 98 (94 to 99.57)  | 99 (93.5 to 99.97) |
| NZ98/254; Day 1 (N=36,105,141,83)  | 0 (0 to 9.7)      | 4 (1 to 9.5)      | 3 (0.8 to 7.1)    | 0 (0 to 4.3)       |
| NZ98/254; Day 91 (N=38,106,144,84) | 63 (46 to 78.2)   | 79 (70.3 to 86.5) | 75 (67.1 to 81.8) | 73 (61.8 to 81.8)  |
| M10713; Day 1 (N=36,102,138,82)    | 47 (30.4 to 64.5) | 68 (57.7 to 76.6) | 62 (53.7 to 70.4) | 68 (57.1 to 78.1)  |
| M10713; Day 91 (N=37,103,140,83)   | 70 (53 to 84.1)   | 94 (87.8 to 97.8) | 88 (81.3 to 92.8) | 98 (91.6 to 99.71) |

## Statistical analyses

No statistical analyses for this end point

### Primary: 3. hSBA Geometric mean titers (GMTs) against N. meningitis serogroup B strains following a 2-dose vaccination schedule.

|                 |  |
|-----------------|--|
| End point title | 3. hSBA Geometric mean titers (GMTs) against N. meningitis serogroup B strains following a 2-dose vaccination schedule. <sup>[3]</sup> |
|-----------------|--|

End point description:

Immunogenicity was assessed in terms of GMTs against N. meningitidis serogroup B indicator strains (H44/76, 5/99, and NZ98/254) and M10713 strain following 2 doses of rMenB+OMV NZ, administered on Day 1 and Day 61. The analysis was done on Full Analysis Set (FAS).

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

End point timeframe:

Day 1 and Day 91 (one month after the second dose of the study vaccine).

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis was associated to this endpoint. Analyses were run descriptively.

| End point values                         | CompDef             | Asplenia            | CompDef+Asplenia    | Healthy Subjects    |
|--|---------------------|---------------------|---------------------|---------------------|
| Subject group type                       | Reporting group     | Reporting group     | Reporting group     | Reporting group     |
| Number of subjects analysed              | 39                  | 106                 | 144                 | 85                  |
| Units: Titers                            |                     |                     |                     |                     |
| geometric mean (confidence interval 95%) |                     |                     |                     |                     |
| H44/76; Day 1 (N=39,104,143,84)          | 1.08 (0.87 to 1.33) | 1.17 (1.03 to 1.32) | 1.14 (1.03 to 1.26) | 1.15 (1.03 to 1.28) |
| H44/76; Day 91 (N=39,104,143,85)         | 48 (29 to 79)       | 65 (48 to 88)       | 60 (46 to 77)       | 76 (61 to 94)       |
| 5/99; Day 1 (N=37,103,140,82)            | 0.87 (0.61 to 1.26) | 1.43 (1.16 to 1.78) | 1.26 (1.05 to 1.51) | 1.24 (1.02 to 1.52) |
| 5/99; Day 91 (N=38,106,144,83)           | 263 (166 to 415)    | 300 (230 to 392)    | 290 (231 to 362)    | 307 (250 to 376)    |

|                                    |                     |                    |                     |                     |
|------------------------------------|---------------------|--------------------|---------------------|---------------------|
| NZ98/254; Day 1 (N=36,105,141,83)  | 0.95 (0.78 to 1.16) | 1.1 (0.98 to 1.24) | 1.06 (0.96 to 1.17) | 1.05 (0.98 to 1.12) |
| NZ98/254; Day 91 (N=38,106,144,84) | 8.46 (4.85 to 15)   | 18 (13 to 24)      | 14 (11 to 19)       | 14 (10 to 18)       |
| M10713; Day 1 (N=36,102,138,82)    | 8.57 (4.43 to 17)   | 15 (10 to 22)      | 13 (9.44 to 18)     | 16 (11 to 22)       |
| M10713; Day 91 (N=37,103,140,83)   | 20 (11 to 34)       | 45 (33 to 62)      | 36 (28 to 47)       | 42 (34 to 52)       |

## Statistical analyses

No statistical analyses for this end point

### Primary: 4. Geometric mean ratios on Day 91 against N. meningitis serogroup B strains following a 2-dose vaccination schedule.

|                 |  |
|-----------------|--|
| End point title | 4. Geometric mean ratios on Day 91 against N. meningitis serogroup B strains following a 2-dose vaccination schedule. <sup>[4]</sup> |
|-----------------|--|

End point description:

Immunogenicity was assessed in terms of geometric mean ratios (GMRs) against N meningitidis serogroup B indicator strains (H44/76, 5/99, and NZ98/254) and M10713 strain following 2 doses of rMenB+OMV NZ, administered on Day 1 and Day 61. The analysis was done on Full Analysis Set (FAS).

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

End point timeframe:

Day 1 and Day 91 (one month after the second dose of the study vaccine).

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis was associated to this endpoint. Analyses were run descriptively.

| End point values                         | CompDef             | Asplenia            | CompDef+Asplenia    | Healthy Subjects    |
|--|---------------------|---------------------|---------------------|---------------------|
| Subject group type                       | Reporting group     | Reporting group     | Reporting group     | Reporting group     |
| Number of subjects analysed              | 39                  | 105                 | 143                 | 84                  |
| Units: Ratios                            |                     |                     |                     |                     |
| geometric mean (confidence interval 95%) |                     |                     |                     |                     |
| H44/76; Day 91/Day 1 (N=39,104,143,84)   | 44 (27 to 73)       | 56 (41 to 75)       | 52 (41 to 67)       | 66 (52 to 83)       |
| 5/99; Day 91/Day 1 (N=37,103,140,82)     | 299 (170 to 525)    | 207 (149 to 288)    | 228 (173 to 302)    | 245 (187 to 321)    |
| NZ98/254; Day 91/Day 1 (N=36,105,141,83) | 8.58 (4.9 to 15)    | 16 (12 to 22)       | 14 (10 to 18)       | 13 (10 to 17)       |
| M10713; Day 91/Day 1 (N=36,102,138,82)   | 2.25 (1.37 to 3.71) | 2.95 (2.21 to 3.95) | 2.75 (2.15 to 3.51) | 2.71 (2.02 to 3.65) |

## Statistical analyses

No statistical analyses for this end point

### Primary: 5. Percentage of subjects with 4-fold increase in hSBA titers against N. meningitis serogroup B strains following a 2-dose vaccination.

|                 |  |
|-----------------|--|
| End point title | 5. Percentage of subjects with 4-fold increase in hSBA titers against N. meningitis serogroup B strains following a 2-dose |
|-----------------|--|

## End point description:

Antibody responses were assessed in terms of percentage of subjects achieving 4-fold increase in hSBA titers against *N. meningitidis* serogroup B indicator strains (H44/76, 5/99, and NZ98/254) and M10713 strain on Day 91 over baseline (Day 1), following 2 doses of rMenB+OMV NZ, administered on Day 1 and Day 61. The analysis was done on Full Analysis Set (FAS).

## End point type

Primary

## End point timeframe:

Day 91 (one month after the second dose of the study vaccine).

## Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis was associated to this endpoint. Analyses were run descriptively.

| End point values                 | CompDef           | Asplenia          | CompDef+Asplenia   | Healthy Subjects   |
|----------------------------------|-------------------|-------------------|--------------------|--------------------|
| Subject group type               | Reporting group   | Reporting group   | Reporting group    | Reporting group    |
| Number of subjects analysed      | 39                | 105               | 143                | 85                 |
| Units: Percentages of Subjects   |                   |                   |                    |                    |
| number (confidence interval 95%) |                   |                   |                    |                    |
| H44/76 (N=39,104,143,84)         | 87 (72.6 to 95.7) | 94 (87.9 to 97.9) | 92 (86.7 to 96.1)  | 98 (91.7 to 99.71) |
| 5/99 (N=37,103,140,82)           | 92 (78.1 to 98.3) | 100 (96.5 to 100) | 98 (93.9 to 99.56) | 98 (91.5 to 99.7)  |
| NZ98/254 (N=36,105,141,83)       | 61 (43.5 to 76.9) | 80 (71.1 to 87.2) | 75 (67.2 to 82.1)  | 73 (62.7 to 82.6)  |
| M10713 (N=36,102,138,82)         | 25 (12.1 to 42.2) | 33 (24.3 to 43.4) | 31 (23.6 to 39.6)  | 33 (22.9 to 44.2)  |

## Statistical analyses

No statistical analyses for this end point

**Primary: 6. Geometric mean concentrations (GMCs) of antibodies against vaccine antigen 287-953 following a 2-dose vaccination schedule.**

## End point title

6. Geometric mean concentrations (GMCs) of antibodies against vaccine antigen 287-953 following a 2-dose vaccination schedule.<sup>[6]</sup>

## End point description:

Immune responses were measured as ELISA GMCs of antibodies against vaccine antigen 287-953 following 2 doses of rMenB+OMV NZ, administered on Day 1 and Day 61. The analysis was done on Full Analysis Set (FAS).

## End point type

Primary

## End point timeframe:

Day 1 and Day 91 (one month after the second dose of the study vaccine).

## Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis was associated to this endpoint. Analyses were run descriptively.

| End point values                             | CompDef             | Asplenia            | CompDef+Asplenia    | Healthy Subjects    |
|--|---------------------|---------------------|---------------------|---------------------|
| Subject group type                           | Reporting group     | Reporting group     | Reporting group     | Reporting group     |
| Number of subjects analysed                  | 40                  | 106                 | 146                 | 84                  |
| Units: Concentrations                        |                     |                     |                     |                     |
| geometric mean (confidence interval 95%)     |                     |                     |                     |                     |
| Antigen 287-953; Day 1<br>(N=39,106,145,84)  | 33 (25 to 43)       | 25 (21 to 29)       | 27 (23 to 31)       | 27 (23 to 31)       |
| Antigen 287-953; Day 91<br>(N=40,106,146,84) | 2039 (1436 to 2894) | 3418 (2780 to 4202) | 2973 (2492 to 3546) | 2957 (2450 to 3570) |

## Statistical analyses

No statistical analyses for this end point

### Primary: 7. ELISA GMRs on Day 91 against vaccine antigen 287-953 following a 2-dose vaccination schedule.

|                 |   |
|-----------------|---|
| End point title | 7. ELISA GMRs on Day 91 against vaccine antigen 287-953 following a 2-dose vaccination schedule. <sup>[7]</sup> |
|-----------------|---|

End point description:

Immune responses were measured as ELISA GMRs against vaccine antigen 287-953 following 2 doses of rMenB+OMV NZ, administered on Day 1 and Day 61. The analysis was done on Full Analysis Set (FAS).

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

End point timeframe:

Day 1 and Day 91 (one month after the second dose of the study vaccine).

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis was associated to this endpoint. Analyses were run descriptively.

| End point values                                  | CompDef         | Asplenia         | CompDef+Asplenia | Healthy Subjects |
|---|-----------------|------------------|------------------|------------------|
| Subject group type                                | Reporting group | Reporting group  | Reporting group  | Reporting group  |
| Number of subjects analysed                       | 39              | 106              | 145              | 84               |
| Units: Ratios                                     |                 |                  |                  |                  |
| geometric mean (confidence interval 95%)          |                 |                  |                  |                  |
| Antigen 287-953 Day 91/Day 1<br>(N=39,106,145,84) | 62 (40 to 97)   | 138 (107 to 178) | 112 (90 to 139)  | 111 (88 to 140)  |

## Statistical analyses

No statistical analyses for this end point

### Primary: 8. Percentage of subjects with 4-fold increase in ELISA concentrations against N. meningitis serogroup B strains following a 2-dose vaccination schedule.

|                 |  |
|-----------------|--|
| End point title | 8. Percentage of subjects with 4-fold increase in ELISA concentrations against N. meningitis serogroup B strains following a 2-dose vaccination schedule. <sup>[8]</sup> |
|-----------------|--|

End point description:

Antibody responses were assessed in terms of percentage of subjects achieving 4-fold increase in ELISA concentrations against vaccine antigen 287-953 on Day 91 over baseline (Day 1), following 2 doses of rMenB+OMV NZ, administered on Day 1 and Day 61. The analysis was done on Full Analysis Set (FAS).

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

End point timeframe:

Day 91 (one month after the second dose of the study vaccine).

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis was associated to this endpoint. Analyses were run descriptively.

| End point values                  | CompDef            | Asplenia           | CompDef+Asplenia   | Healthy Subjects   |
|-----------------------------------|--------------------|--------------------|--------------------|--------------------|
| Subject group type                | Reporting group    | Reporting group    | Reporting group    | Reporting group    |
| Number of subjects analysed       | 39                 | 106                | 146                | 84                 |
| Units: Percentages of Subjects    |                    |                    |                    |                    |
| number (confidence interval 95%)  |                    |                    |                    |                    |
| Antigen 287-953 (N=39,106,145,84) | 97 (86.5 to 99.94) | 98 (93.4 to 99.77) | 98 (94.1 to 99.57) | 98 (91.7 to 99.71) |

## Statistical analyses

No statistical analyses for this end point

## Primary: 9. Number Of Subjects With Solicited Local or Systemic Adverse Events.

|                 |   |
|-----------------|---|
| End point title | 9. Number Of Subjects With Solicited Local or Systemic Adverse Events. <sup>[9]</sup> |
|-----------------|---|

End point description:

Safety was assessed as the number of subjects who reported solicited local or systemic adverse events (AEs) following administration of rMenB+OMV NZ vaccine. The analysis was done on the Solicited Safety Set.

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

End point timeframe:

Day 1 through Day 7 after any vaccination.

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis was associated to this endpoint. Analyses were run descriptively.

| End point values                                  | CompDef         | Asplenia        | CompDef+Asplenia | Healthy Subjects   |
|---|-----------------|-----------------|------------------|--------------------|
| Subject group type                                | Reporting group | Reporting group | Reporting group  | Reporting group    |
| Number of subjects analysed                       | 28              | 100             | 128              | 74 <sup>[10]</sup> |
| Units: Subjects                                   |                 |                 |                  |                    |
| Any Local (< 6 years; N=12,9,21,13)               | 12              | 6               | 18               | 12                 |
| Injection Site Tendern. (< 6 years; N=12,9,21,13) | 12              | 6               | 18               | 12                 |
| Injection Site Erythema (< 6 years; N=12,9,21,13) | 7               | 4               | 11               | 6                  |
| Injection Site Indur. (< 6 years; N=12,9,21,13)   | 5               | 4               | 9                | 5                  |

|   |    |    |     |    |
|---|----|----|-----|----|
| Any Local ( $\geq 6$ years)   | 26 | 98 | 124 | 74 |
| Injection Site Pain ( $\geq 6$ years)                               | 25 | 97 | 122 | 71 |
| Injection Site Erythema ( $\geq 6$ years)                           | 7  | 19 | 26  | 27 |
| Injection Site Swelling ( $\geq 6$ years)                           | 8  | 24 | 32  | 24 |
| Injection Site Indur. ( $\geq 6$ years)                             | 11 | 27 | 38  | 19 |
| Any Systemic ( $< 6$ years)   | 11 | 6  | 17  | 12 |
| Change in Eating Habits ( $< 6$ years;<br>N=12,9,21,13)             | 5  | 1  | 6   | 8  |
| Persistent Crying ( $< 6$ years;<br>N=12,9,21,13)                   | 2  | 2  | 4   | 6  |
| Irritability ( $< 6$ years; N=12,9,21,13)                           | 6  | 2  | 8   | 9  |
| Vomiting ( $< 6$ years; N=12,9,21,13)                               | 2  | 0  | 2   | 0  |
| Diarrhea ( $< 6$ years; N=12,9,21,13)                               | 5  | 3  | 8   | 3  |
| Fever ( $\geq 38^{\circ}\text{C}$ ) ( $< 6$ years;<br>N=12,9,21,13) | 3  | 1  | 4   | 4  |
| Rash ( $< 6$ years; N=12,9,21,13)                                   | 3  | 0  | 3   | 0  |
| Any Others ( $< 6$ years; N=12,9,21,13)                             | 12 | 8  | 20  | 13 |
| Prev. Pain/Fever ( $< 6$ years;<br>N=12,9,21,13)                    | 5  | 1  | 6   | 4  |
| Use of Analg./Antipyr. ( $< 6$ years;<br>N=12,9,21,13)              | 5  | 3  | 8   | 11 |
| Any Systemic ( $\geq 6$ years)                                      | 21 | 75 | 96  | 60 |
| Nausea ( $\geq 6$ years)  | 7  | 28 | 35  | 15 |
| Fatigue ( $\geq 6$ years)   | 11 | 55 | 66  | 46 |
| Myalgia ( $\geq 6$ years)   | 8  | 31 | 39  | 27 |
| Arthralgia ( $\geq 6$ years)  | 7  | 25 | 32  | 18 |
| Headache ( $\geq 6$ years)  | 11 | 47 | 58  | 35 |
| Fever ( $\geq 38^{\circ}\text{C}$ ) ( $\geq 6$ years)               | 6  | 6  | 12  | 5  |
| Rash ( $\geq 6$ years)  | 7  | 9  | 16  | 6  |
| Prev. Pain/Fever ( $\geq 6$ years)                                  | 5  | 9  | 14  | 15 |
| Use of Analg./Antipyr. ( $\geq 6$ years)                            | 14 | 39 | 53  | 38 |
| Any Others ( $\geq 6$ years)  | 27 | 98 | 125 | 74 |
| Sleepiness ( $< 6$ years; N=12,9,21,13)                             | 7  | 3  | 10  | 5  |
| Injection Site Swelling ( $< 6$ years;<br>N=12,9,21,13)             | 6  | 4  | 10  | 6  |

Notes:

[10] - Only for Myalgia ( $\geq 6$  years) N = 28,100,128,73.

## Statistical analyses

No statistical analyses for this end point

## Primary: 10. Number Of Subjects With Unsolicited Adverse Events.

|                 |   |
|-----------------|---|
| End point title | 10. Number Of Subjects With Unsolicited Adverse Events. <sup>[11]</sup> |
|-----------------|---|

End point description:

Safety was assessed as the number of subjects who reported unsolicited AEs collected from Day 1 through Day 7 after any vaccination; serious adverse events (SAEs), AEs leading to withdrawal and medically attended AEs were collected throughout the study period. The analysis was done on the Unsolicited Safety Set.

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

End point timeframe:

Day 1 through Day 7 after any vaccination; throughout the study period.

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis was associated to this endpoint. Analyses were run descriptively.

| <b>End point values</b>                   | CompDef         | Asplenia        | CompDef+Asplenia | Healthy Subjects |
|---|-----------------|-----------------|------------------|------------------|
| Subject group type                        | Reporting group | Reporting group | Reporting group  | Reporting group  |
| Number of subjects analysed               | 40              | 110             | 150              | 87               |
| Units: Subjects                           |                 |                 |                  |                  |
| Any AE                                    | 17              | 38              | 55               | 34               |
| At least possibly related unsolicited AEs | 9               | 19              | 28               | 18               |
| Any SAEs                                  | 1               | 5               | 6                | 0                |
| At least Possibly Related SAEs            | 0               | 0               | 0                | 0                |
| AEs leading to death                      | 0               | 0               | 0                | 0                |
| AEs Leading to Withdrawal                 | 0               | 1               | 1                | 0                |
| MEdically Attended AEs                    | 13              | 26              | 39               | 18               |

### Statistical analyses

No statistical analyses for this end point



## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Throughout the study period.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 18.1 |
|--------------------|------|

### Reporting groups

|                       |         |
|-----------------------|---------|
| Reporting group title | CompDef |
|-----------------------|---------|

Reporting group description:

Subjects aged  $\geq 2$  to  $\leq 17$  years with complement deficiencies received 2 doses of rMenB+OMV NZ administered 2 months apart.

|                       |          |
|-----------------------|----------|
| Reporting group title | Asplenia |
|-----------------------|----------|

Reporting group description:

Subjects aged  $\geq 2$  to  $\leq 17$  years with Asplenia received 2 doses of rMenB+OMV NZ administered 2 months apart.

|                       |                    |
|-----------------------|--------------------|
| Reporting group title | CompDef + Asplenia |
|-----------------------|--------------------|

Reporting group description:

Subjects aged  $\geq 2$  to  $\leq 17$  years with either complement deficiencies or Asplenia received 2 doses of rMenB+OMV NZ administered 2 months apart.

|                       |                  |
|-----------------------|------------------|
| Reporting group title | Healthy Subjects |
|-----------------------|------------------|

Reporting group description:

Healthy subjects aged  $\geq 2$  to  $\leq 17$  years received 2 doses of rMenB+OMV NZ administered 2 months apart.

| Serious adverse events                            | CompDef        | Asplenia        | CompDef + Asplenia |
|---|----------------|-----------------|--------------------|
| Total subjects affected by serious adverse events |                |                 |                    |
| subjects affected / exposed                       | 1 / 40 (2.50%) | 5 / 110 (4.55%) | 6 / 150 (4.00%)    |
| number of deaths (all causes)                     | 0              | 0               | 0                  |
| number of deaths resulting from adverse events    | 0              | 0               | 0                  |
| Injury, poisoning and procedural complications    |                |                 |                    |
| Concussion  |                |                 |                    |
| subjects affected / exposed                       | 0 / 40 (0.00%) | 1 / 110 (0.91%) | 1 / 150 (0.67%)    |
| occurrences causally related to treatment / all   | 0 / 0          | 0 / 1           | 0 / 1              |
| deaths causally related to treatment / all        | 0 / 0          | 0 / 0           | 0 / 0              |
| Cardiac disorders                                 |                |                 |                    |
| Intracardiac thrombus                             |                |                 |                    |
| subjects affected / exposed                       | 0 / 40 (0.00%) | 1 / 110 (0.91%) | 1 / 150 (0.67%)    |
| occurrences causally related to treatment / all   | 0 / 0          | 0 / 1           | 0 / 1              |
| deaths causally related to treatment / all        | 0 / 0          | 0 / 0           | 0 / 0              |

|   |                |                 |                 |
|---|----------------|-----------------|-----------------|
| Respiratory, thoracic and mediastinal disorders |                |                 |                 |
| Respiratory disorder                            |                |                 |                 |
| subjects affected / exposed                     | 0 / 40 (0.00%) | 1 / 110 (0.91%) | 1 / 150 (0.67%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Infections and infestations                     |                |                 |                 |
| Appendicitis                                    |                |                 |                 |
| subjects affected / exposed                     | 0 / 40 (0.00%) | 1 / 110 (0.91%) | 1 / 150 (0.67%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Gastroenteritis salmonella                      |                |                 |                 |
| subjects affected / exposed                     | 0 / 40 (0.00%) | 1 / 110 (0.91%) | 1 / 150 (0.67%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Respiratory tract infection viral               |                |                 |                 |
| subjects affected / exposed                     | 1 / 40 (2.50%) | 0 / 110 (0.00%) | 1 / 150 (0.67%) |
| occurrences causally related to treatment / all | 0 / 1          | 0 / 0           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |
| Tonsillitis                                     |                |                 |                 |
| subjects affected / exposed                     | 0 / 40 (0.00%) | 1 / 110 (0.91%) | 1 / 150 (0.67%) |
| occurrences causally related to treatment / all | 0 / 0          | 0 / 1           | 0 / 1           |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0           | 0 / 0           |

|   |                  |  |  |
|---|------------------|--|--|
| <b>Serious adverse events</b>                     | Healthy Subjects |  |  |
| Total subjects affected by serious adverse events |                  |  |  |
| subjects affected / exposed                       | 0 / 87 (0.00%)   |  |  |
| number of deaths (all causes)                     | 0                |  |  |
| number of deaths resulting from adverse events    | 0                |  |  |
| Injury, poisoning and procedural complications    |                  |  |  |
| Concussion  |                  |  |  |
| subjects affected / exposed                       | 0 / 87 (0.00%)   |  |  |
| occurrences causally related to treatment / all   | 0 / 0            |  |  |
| deaths causally related to treatment / all        | 0 / 0            |  |  |
| Cardiac disorders                                 |                  |  |  |
| Intracardiac thrombus                             |                  |  |  |

|   |                |  |  |
|---|----------------|--|--|
| subjects affected / exposed                     | 0 / 87 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Respiratory, thoracic and mediastinal disorders |                |  |  |
| Respiratory disorder                            |                |  |  |
| subjects affected / exposed                     | 0 / 87 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Infections and infestations                     |                |  |  |
| Appendicitis                                    |                |  |  |
| subjects affected / exposed                     | 0 / 87 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Gastroenteritis salmonella                      |                |  |  |
| subjects affected / exposed                     | 0 / 87 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Respiratory tract infection viral               |                |  |  |
| subjects affected / exposed                     | 0 / 87 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |
| Tonsillitis                                     |                |  |  |
| subjects affected / exposed                     | 0 / 87 (0.00%) |  |  |
| occurrences causally related to treatment / all | 0 / 0          |  |  |
| deaths causally related to treatment / all      | 0 / 0          |  |  |

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

| Non-serious adverse events                            | CompDef          | Asplenia           | CompDef + Asplenia |
|---|------------------|--------------------|--------------------|
| Total subjects affected by non-serious adverse events |                  |                    |                    |
| subjects affected / exposed                           | 39 / 40 (97.50%) | 106 / 110 (96.36%) | 145 / 150 (96.67%) |
| Nervous system disorders                              |                  |                    |                    |
| Headache  |                  |                    |                    |

|   |                        |                           |                           |
|---|------------------------|---------------------------|---------------------------|
| subjects affected / exposed<br>occurrences (all)                              | 11 / 40 (27.50%)<br>15 | 48 / 110 (43.64%)<br>70   | 59 / 150 (39.33%)<br>85   |
| Somnolence<br>subjects affected / exposed<br>occurrences (all)                | 7 / 40 (17.50%)<br>11  | 3 / 110 (2.73%)<br>4      | 10 / 150 (6.67%)<br>15    |
| General disorders and administration<br>site conditions                       |                        |                           |                           |
| Fatigue<br>subjects affected / exposed<br>occurrences (all)                   | 11 / 40 (27.50%)<br>19 | 55 / 110 (50.00%)<br>89   | 66 / 150 (44.00%)<br>108  |
| Injection site erythema<br>subjects affected / exposed<br>occurrences (all)   | 15 / 40 (37.50%)<br>18 | 23 / 110 (20.91%)<br>34   | 38 / 150 (25.33%)<br>52   |
| Injection site induration<br>subjects affected / exposed<br>occurrences (all) | 17 / 40 (42.50%)<br>30 | 32 / 110 (29.09%)<br>48   | 49 / 150 (32.67%)<br>78   |
| Injection site pain<br>subjects affected / exposed<br>occurrences (all)       | 37 / 40 (92.50%)<br>72 | 103 / 110 (93.64%)<br>196 | 140 / 150 (93.33%)<br>268 |
| Injection site swelling<br>subjects affected / exposed<br>occurrences (all)   | 14 / 40 (35.00%)<br>23 | 28 / 110 (25.45%)<br>45   | 42 / 150 (28.00%)<br>68   |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)                   | 10 / 40 (25.00%)<br>11 | 7 / 110 (6.36%)<br>9      | 17 / 150 (11.33%)<br>20   |
| Gastrointestinal disorders  |                        |                           |                           |
| Nausea<br>subjects affected / exposed<br>occurrences (all)                    | 7 / 40 (17.50%)<br>12  | 28 / 110 (25.45%)<br>42   | 35 / 150 (23.33%)<br>54   |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)                 | 5 / 40 (12.50%)<br>5   | 4 / 110 (3.64%)<br>6      | 9 / 150 (6.00%)<br>11     |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)                  | 3 / 40 (7.50%)<br>3    | 0 / 110 (0.00%)<br>0      | 3 / 150 (2.00%)<br>3      |
| Skin and subcutaneous tissue disorders  |                        |                           |                           |

|   |                        |                         |                         |
|---|------------------------|-------------------------|-------------------------|
| Rash<br>subjects affected / exposed<br>occurrences (all)  | 10 / 40 (25.00%)<br>12 | 9 / 110 (8.18%)<br>10   | 19 / 150 (12.67%)<br>22 |
| Psychiatric disorders<br>Eating disorder<br>subjects affected / exposed<br>occurrences (all)                      | 5 / 40 (12.50%)<br>8   | 1 / 110 (0.91%)<br>1    | 6 / 150 (4.00%)<br>9    |
| Irritability<br>subjects affected / exposed<br>occurrences (all)  | 7 / 40 (17.50%)<br>14  | 2 / 110 (1.82%)<br>5    | 9 / 150 (6.00%)<br>19   |
| Musculoskeletal and connective tissue disorders<br>Arthralgia<br>subjects affected / exposed<br>occurrences (all) | 7 / 40 (17.50%)<br>11  | 25 / 110 (22.73%)<br>38 | 32 / 150 (21.33%)<br>49 |
| Myalgia<br>subjects affected / exposed<br>occurrences (all)   | 8 / 40 (20.00%)<br>13  | 31 / 110 (28.18%)<br>44 | 39 / 150 (26.00%)<br>57 |

|   |                        |  |  |
|---|------------------------|--|--|
| <b>Non-serious adverse events</b>   | Healthy Subjects       |  |  |
| Total subjects affected by non-serious adverse events<br>subjects affected / exposed                                | 87 / 87 (100.00%)      |  |  |
| Nervous system disorders<br>Headache<br>subjects affected / exposed<br>occurrences (all)                            | 35 / 87 (40.23%)<br>59 |  |  |
| Somnolence<br>subjects affected / exposed<br>occurrences (all)  | 5 / 87 (5.75%)<br>7    |  |  |
| General disorders and administration site conditions<br>Fatigue<br>subjects affected / exposed<br>occurrences (all) | 46 / 87 (52.87%)<br>67 |  |  |
| Injection site erythema<br>subjects affected / exposed<br>occurrences (all)   | 34 / 87 (39.08%)<br>49 |  |  |
| Injection site induration   |                        |  |  |

|  |  |  |  |
|--|--|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Injection site pain</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Injection site swelling</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Pyrexia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>26 / 87 (29.89%)</p> <p>36</p> <p>83 / 87 (95.40%)</p> <p>171</p> <p>32 / 87 (36.78%)</p> <p>46</p> <p>10 / 87 (11.49%)</p> <p>11</p> |  |  |
| <p>Gastrointestinal disorders</p> <p>Nausea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Diarrhoea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Vomiting</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>   | <p>15 / 87 (17.24%)</p> <p>21</p> <p>4 / 87 (4.60%)</p> <p>6</p> <p>0 / 87 (0.00%)</p> <p>0</p>  |  |  |
| <p>Skin and subcutaneous tissue disorders</p> <p>Rash</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>6 / 87 (6.90%)</p> <p>8</p>   |  |  |
| <p>Psychiatric disorders</p> <p>Eating disorder</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Irritability</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>  | <p>8 / 87 (9.20%)</p> <p>13</p> <p>9 / 87 (10.34%)</p> <p>14</p>   |  |  |
| <p>Musculoskeletal and connective tissue disorders</p> <p>Arthralgia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p>   | <p>18 / 87 (20.69%)</p> <p>24</p>  |  |  |

|                             |                  |  |  |
|-----------------------------|------------------|--|--|
| Myalgia                     |                  |  |  |
| subjects affected / exposed | 27 / 87 (31.03%) |  |  |
| occurrences (all)           | 34               |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date         | Amendment   |
|--------------|---|
| 30 July 2014 | <p>The first version of the protocol was issued on June 20, 2013 and subsequently 3 amendments were issued. A total of 2 protocol amendments were issued before FSFV and</p> <p>1 was issued after FSFV:</p> <ul style="list-style-type: none"><li>- Amendment 1 was issued on July 22, 2013 and occurred before any clinical trial application and aims to correct minor inconsistencies, was classified as non-substantial;</li><li>- Amendment 2 was issued on October 16, 2013 and occurred before any clinical trial application and after the review of clinical study protocol by the Committee for Medicinal Products for Human Use (CHMP). It included feedback and recommendation from the CHMP, was classified as substantial;</li><li>- Amendment 3 was issued on July 30, 2014 it occurred after FSFV and it was classified as substantial: Amendment no 3 of protocol was issued to allow for additional study participants. Although the additional participants allowed for greater precision in the estimation of the study parameters, the sample size for this study was driven by feasibility and regulatory considerations, and not by formal statistical assumptions. Thus, no changes in the analysis and interpretation of results were foreseen. The protocol amendment permitted the screening of subjects who have already been booked in the UK, as per recommendation of a local EC, as well as the participation of subjects in Russian centers which had received Health Authority approval after the preamendment enrollment target for patients at increased risk of meningococcal disease had been reached. According to clinical study protocol amendment no 3, approximately 240 subjects (ie, up to 160 patients at increased risk of meningococcal disease and approximately 80 matched healthy subjects) meeting all eligibility criteria were to be enrolled.</li></ul> |

Notes:

---

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported