# Clinical trial results:
# A Phase IIIB, Randomized, Observer-blind, Multicenter Study to Assess the Safety and Immunogenicity of GSK's Meningococcal Group B Vaccine When Administered Concomitantly With GSK's Meningococcal MenACWY Conjugate Vaccine to Healthy Subjects of 16-18 Years of Age

## Summary

| | |
|---|---|
| EudraCT number | 2016-003722-16 |
| Trial protocol | Outside EU/EEA IT |
| Global end of trial date | 22 July 2024 |

### Results information

| | |
|---|---|
| Result version number | v2 (current) |
| This version publication date | 03 May 2025 |
| First version publication date | 02 February 2025 |
| Version creation reason | • Correction of full data set<br>Few correction made on the summary |

## Trial information

### Trial identification

| | |
|---|---|
| Sponsor protocol code | 205419 |

### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04318548 |
| WHO universal trial number (UTN) | - |

Notes:

### Sponsors

| | |
|---|---|
| Sponsor organisation name | GlaxoSmithKline |
| Sponsor organisation address | Rue de l'Institut, 89,, Rixensart, Belgium, 1330 |
| Public contact | GSK Response Center, GlaxoSmithKline, 044 8664357343, GSKClinicalSupportHD@gsk.com |
| Scientific contact | GSK Response Center, GlaxoSmithKline, 044 8664357343, GSKClinicalSupportHD@gsk.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 | 03 October 2024 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 21 November 2023 |
| Global end of trial reached? | Yes |
| Global end of trial date | 22 July 2024 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

• To assess the safety and tolerability of rMenB+OMV NZ and MenACWY, when administered concomitantly or alone, in healthy subjects 16-18 years of age.
• To demonstrate the non-inferiority of the antibody response to rMenB+OMV NZ given concomitantly with MenACWY to healthy subjects 16-18 years of age compared to rMenB+OMV NZ administered alone, as measured by serum bactericidal assay using human complement (hSBA) Geometric Mean Titers (GMTs) against N. meningitidis serogroup B indicator strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA) and M07-0241084 (NHBA), at 1 month after the second vaccination with rMenB+OMV NZ.
• To demonstrate the non-inferiority of the antibody response to MenACWY given concomitantly with rMenB+OMV NZ to healthy subjects 16-18 years of age compared to MenACWY administered alone, as measured by hSBA GMTs against each of the N. meningitidis serogroups A, C, W and Y, at 1 month after the (study) vaccination with MenACWY.

Protection of trial subjects:

Vaccine administration was preceded by a review of the subjects' medical history (including previous vaccination and occurrence of undesirable events) and a general physical examination at the first visit and symptom-directed physical examination before subsequent vaccinations. Protocol procedures, including blood sampling, were done by a qualified healthcare professional. The subjects were observed closely for at least 30 minutes following the administration of the vaccine(s)/product(s), with appropriate medical treatment readily available in case of anaphylaxis and syncope.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 25 August 2020 |
| 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 | Italy: 111 |
| Country: Number of subjects enrolled | United States: 834 |
| Worldwide total number of subjects | 945 |
| EEA total number of subjects | 111 |

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) | 864 |
| Adults (18-64 years) | 81 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

The study ended on Day 271 for participants who had not reached Day 271 when Protocol Amendment 7 took effect, and on Day 451 for those who had already passed Day 271.Safety follow-up period for each participant was from Day 1 up to Day 451 or Day 271 for participants who have not reached Day 271 at the time Protocol Amendment 7 took effect.

### Pre-assignment

Screening details:

A total of 945 participants were enrolled in the study, of which only 940 were randomized into the 3 treatment groups. After randomization, 2 participants did not receive the vaccine and making it a total of 938 participants in the exposed set.

### Period 1

| | |
|---|---|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Monitor, Data analyst, Subject, Investigator |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | MenB+MenACWY Group |

Arm description:

Participants received 1 dose of rMenB+OMV NZ vaccine administered concomitantly with 1 dose of MenACWY vaccine, as separate injections in each arm at Day 1, 1 dose of rMenB+OMV NZ vaccine at Day 61 and 1 dose of placebo at Day 91.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | rMenB+OMV NZ |
| Investigational medicinal product code | |
| Other name | Bexsero |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

2 dose of rMenB+OMV NZ vaccine administered intramuscularly.

| | |
|---|---|
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Intramuscular use |

Dosage and administration details:

1 dose of Placebo administered intramuscularly.

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

Dosage and administration details:

1 dose of MenACWY vaccine administered intramuscularly.

| | |
|---|---|
| **Arm title** | MenB Group |

Arm description:

Participants received 1 dose of rMenB+OMV NZ vaccine administered concomitantly with 1 dose of

placebo, as separate injections in each arm at Day 1, 1 dose of rMenB+OMV NZ vaccine at Day 61 and 1 dose of MenACWY at Day 91.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | rMenB+OMV NZ |
| Investigational medicinal product code | |
| Other name | Bexsero |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

2 dose of rMenB+OMV NZ vaccine administered intramuscularly.

| | |
|---|---|
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Intramuscular use |

Dosage and administration details:

1 dose of Placebo administered intramuscularly.

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

Dosage and administration details:

1 dose of MenACWY vaccine administered intramuscularly.

| | |
|---|---|
| **Arm title** | MenACWY Group |

Arm description:

Participants received 1 dose of MenACWY vaccine administered concomitantly with 1 dose of placebo, as separate injections in each arm at Day1, 1 dose of rMenB+OMV NZ vaccine each administered at Day 61 and at Day 91.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | rMenB+OMV NZ |
| Investigational medicinal product code | |
| Other name | Bexsero |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

2 dose of rMenB+OMV NZ vaccine administered intramuscularly.

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

Dosage and administration details:

1 dose of MenACWY vaccine administered intramuscularly.

| | |
|---|---|
| Investigational medicinal product name | Placebo |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection in pre-filled syringe |
| Routes of administration | Intramuscular use |

Dosage and administration details:

1 dose of Placebo administered intramuscularly.

| **Number of subjects in period 1[1]** | MenB+MenACWY Group | MenB Group | MenACWY Group |
|---|---|---|---|
| Started | 310 | 308 | 320 |
| Completed | 297 | 284 | 298 |
| Not completed | 13 | 24 | 22 |
| Adverse event, non-fatal | - | - | 1 |
| Migrated / moved from the study area | - | - | 1 |
| Not specified | 1 | 2 | 3 |
| Lost to follow-up | 6 | 13 | 9 |
| Consent withdrawal, not due to a (S)AE | 5 | 9 | 6 |
| Protocol deviation | 1 | - | 2 |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: A total of 945 participants were enrolled in the study, of which only 940 were randomized into the 3 treatment groups. After randomization, 2 participants did not receive the vaccine and making it a total of 938 participants in the exposed set.

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | MenB+MenACWY Group |
| Reporting group description: | |
| Participants received 1 dose of rMenB+OMV NZ vaccine administered concomitantly with 1 dose of MenACWY vaccine, as separate injections in each arm at Day 1, 1 dose of rMenB+OMV NZ vaccine at Day 61 and 1 dose of placebo at Day 91. | |
| Reporting group title | MenB Group |
| Reporting group description: | |
| Participants received 1 dose of rMenB+OMV NZ vaccine administered concomitantly with 1 dose of placebo, as separate injections in each arm at Day 1, 1 dose of rMenB+OMV NZ vaccine at Day 61 and 1 dose of MenACWY at Day 91. | |
| Reporting group title | MenACWY Group |
| Reporting group description: | |
| Participants received 1 dose of MenACWY vaccine administered concomitantly with 1 dose of placebo, as separate injections in each arm at Day1, 1 dose of rMenB+OMV NZ vaccine each administered at Day 61 and at Day 91. | |

| Reporting group values | MenB+MenACWY Group | MenB Group | MenACWY Group |
|---|---|---|---|
| Number of subjects | 310 | 308 | 320 |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 0 | 0 | 0 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 286 | 283 | 288 |
| Adults (18-64 years) | 24 | 25 | 32 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age Continuous<br>Units: years | | | |
| arithmetic mean | 16.4 | 16.4 | 16.5 |
| standard deviation | ± 0.7 | ± 0.7 | ± 0.7 |
| Sex: Female, Male<br>Units: Participants | | | |
| Male | 154 | 170 | 157 |
| Female | 156 | 138 | 163 |
| Ethnicity (NIH/OMB)<br>Units: Subjects | | | |
| Hispanic or Latino | 46 | 38 | 37 |
| Not Hispanic or Latino | 263 | 270 | 282 |
| Unknown or Not Reported | 1 | 0 | 1 |

| Reporting group values | Total | | |
|---|---|---|---|
| Number of subjects | 938 | | |

| | | | |
|---|---|---|---|
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | | |
| Newborns (0-27 days) | 0 | | |
| Infants and toddlers (28 days-23 months) | 0 | | |
| Children (2-11 years) | 0 | | |
| Adolescents (12-17 years) | 857 | | |
| Adults (18-64 years) | 81 | | |
| From 65-84 years | 0 | | |
| 85 years and over | 0 | | |
| Age Continuous<br>Units: years | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Sex: Female, Male<br>Units: Participants | | | |
| Male | 481 | | |
| Female | 457 | | |
| Ethnicity (NIH/OMB)<br>Units: Subjects | | | |
| Hispanic or Latino | 121 | | |
| Not Hispanic or Latino | 815 | | |
| Unknown or Not Reported | 2 | | |

## End points

### End points reporting groups

| Reporting group title | MenB+MenACWY Group |
|---|---|
| Reporting group description: | |
| Participants received 1 dose of rMenB+OMV NZ vaccine administered concomitantly with 1 dose of MenACWY vaccine, as separate injections in each arm at Day 1, 1 dose of rMenB+OMV NZ vaccine at Day 61 and 1 dose of placebo at Day 91. | |
| Reporting group title | MenB Group |
| Reporting group description: | |
| Participants received 1 dose of rMenB+OMV NZ vaccine administered concomitantly with 1 dose of placebo, as separate injections in each arm at Day 1, 1 dose of rMenB+OMV NZ vaccine at Day 61 and 1 dose of MenACWY at Day 91. | |
| Reporting group title | MenACWY Group |
| Reporting group description: | |
| Participants received 1 dose of MenACWY vaccine administered concomitantly with 1 dose of placebo, as separate injections in each arm at Day1, 1 dose of rMenB+OMV NZ vaccine each administered at Day 61 and at Day 91. | |

### Primary: Number of participants with solicited local adverse events (AEs) after the vaccination with rMenB+OMV NZ at Day 1

| End point title | Number of participants with solicited local adverse events (AEs) after the vaccination with rMenB+OMV NZ at Day 1[1] |
|---|---|
| End point description: | |
| Solicited local adverse events assessed are injection site pain, erythema, swelling, induration. Any solicited local AEs = occurrence of the symptom regardless of intensity grade. Analysis was performed on the Exposed set (ES), which included all participants who received at least one dose of the study treatment and had the electronic diary (eDiary) for solicited events completed after the administration of study treatment and for whom data were available during the specified period. Allocation per group is based on the treatment administered. Only participants with data available at specified timepoints were included in the analysis. | |
| End point type | Primary |
| End point timeframe: | |
| During 7 days after the rMenB+OMV NZ vaccination at Day 1 | |

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: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| End point values | MenB+MenACWY Group | MenB Group | MenACWY Group | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 307 | 306 | 0[2] | |
| Units: Participants | | | | |
| Erythema | 12 | 12 | | |
| Induration | 14 | 22 | | |
| Pain | 246 | 247 | | |
| Swelling | 15 | 18 | | |

Notes:

[2] - Participants in this group did not receive rMenB+OMV NZ on Day 1 hence zero participants.

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of participants with solicited local adverse events (AEs) after the vaccination with rMenB+OMV NZ at Day 61

| End point title | Number of participants with solicited local adverse events (AEs) after the vaccination with rMenB+OMV NZ at Day 61[3] |
|---|---|

End point description:

Solicited local adverse events assessed are injection site pain, erythema, swelling, induration. Any solicited local AEs = occurrence of the symptom regardless of intensity grade. Analysis was performed on the Exposed set (ES), which included all participants who received at least one dose of the study treatment and had the electronic diary (eDiary) for solicited events completed after the administration of study treatment and for whom data were available during the specified period. Allocation per group is based on the treatment administered. Only participants with data available at specified timepoints were included in the analysis.

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

End point timeframe:

During 7 days after the rMenB+OMV NZ vaccination at Day 61

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: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| **End point values** | MenB+MenACWY Group | MenB Group | MenACWY Group | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 283 | 269 | 287 | |
| Units: Participants | | | | |
| Erythema | 17 | 17 | 8 | |
| Induration | 18 | 19 | 6 | |
| Pain | 240 | 228 | 238 | |
| Swelling | 16 | 16 | 7 | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of participants with solicited local adverse events (AEs) after the vaccination with rMenB+OMV NZ at Day 91

| End point title | Number of participants with solicited local adverse events (AEs) after the vaccination with rMenB+OMV NZ at Day 91[4] |
|---|---|

End point description:

Solicited local adverse events assessed are injection site pain, erythema, swelling, induration. Any solicited local AEs = occurrence of the symptom regardless of intensity grade. Analysis was performed on the Exposed set (ES), which included all participants who received at least one dose of the study treatment and had the electronic diary (eDiary) for solicited events completed after the administration of study treatment and for whom data were available during the specified period. Allocation per group is based on the treatment administered. Only participants with data available at specified timepoints were included in the analysis.

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

End point timeframe:

During 7 days after the rMenB+OMV NZ vaccination at Day 91

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: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| **End point values** | MenB+MenACWY Group | MenB Group | MenACWY Group | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0[5] | 0[6] | 269 | |
| Units: Participants | | | | |
| Erythema | | | 14 | |
| Induration | | | 11 | |
| Pain | | | 205 | |
| Swelling | | | 13 | |

Notes:

[5] - Participants in this group did not receive rMenB+OMV NZ on Day 91 hence zero participants.

[6] - Participants in this group did not receive rMenB+OMV NZ on Day 91 hence zero participants.

### Statistical analyses

No statistical analyses for this end point

## Primary: Number of participants with solicited local AEs after the vaccination with MenACWY at Day 61

| End point title | Number of participants with solicited local AEs after the vaccination with MenACWY at Day 61[7] |
|---|---|

End point description:

Solicited local adverse events assessed are injection site pain, erythema, swelling, induration. Any solicited local AEs= occurrence of the symptom regardless of intensity grade. Analysis was performed on ES population. Only participants with data available at specified timepoints were included in the analysis. 1 participant in MenB Group received wrong study treatment at Day 61 (MenACWY vaccine instead of rMenB+OMV NZ), hence was considered in the analysis population.

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

End point timeframe:

During 7 days after the MenACWY vaccination at Day 61

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: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| **End point values** | MenB+MenACWY Group | MenB Group | MenACWY Group | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0[8] | 1 | 0[9] | |
| Units: Participants | | | | |
| Erythema | | 0 | | |
| Induration | | 0 | | |
| Pain | | 1 | | |
| Swelling | | 0 | | |

Notes:

[8] - Participants in this group did not receive MenACWY on Day 61 hence zero participants.

[9] - Participants in this group did not receive MenACWY on Day 61 hence zero participants.

### Statistical analyses

No statistical analyses for this end point

## Primary: Number of participants with solicited local AEs after the vaccination with MenACWY at Day 1

| End point title | Number of participants with solicited local AEs after the vaccination with MenACWY at Day 1[10] |
|---|---|

End point description:

Solicited local adverse events assessed are injection site pain, erythema, swelling, induration. Any solicited local AEs= occurrence of the symptom regardless of intensity grade. Analysis was performed on ES population. Only participants with data available at specified timepoints were included in the analysis.

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

End point timeframe:

During 7 days after the MenACWY vaccination at Day 1

Notes:

[10] - 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: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| End point values | MenB+MenACWY Group | MenB Group | MenACWY Group | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 307 | 0[11] | 319 | |
| Units: Participants | | | | |
| Erythema | 5 | | 6 | |
| Induration | 7 | | 7 | |
| Pain | 93 | | 104 | |
| Swelling | 5 | | 5 | |

Notes:

[11] - Participants in this group did not receive MenACWY on Day 1 hence zero participants.

### Statistical analyses

No statistical analyses for this end point

## Primary: Number of participants with solicited local AEs after the vaccination with MenACWY at Day 91

| End point title | Number of participants with solicited local AEs after the vaccination with MenACWY at Day 91[12] |
|---|---|

End point description:

Solicited local adverse events assessed are injection site pain, erythema, swelling, induration. Any solicited local AEs= occurrence of the symptom regardless of intensity grade. Analysis was performed on ES population. Only participants with data available at specified timepoints were included in the analysis.

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

End point timeframe:

During 7 days after the MenACWY vaccination at Day 91

Notes:

[12] - 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: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| End point values | MenB+MenACWY Group | MenB Group | MenACWY Group | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0[13] | 265 | 0[14] | |
| Units: Participants | | | | |
| Erythema | | 4 | | |
| Induration | | 1 | | |
| Pain | | 38 | | |
| Swelling | | 5 | | |

Notes:

[13] - Participants in this group did not receive MenACWY on Day 91 hence zero participants.

[14] - Participants in this group did not receive MenACWY on Day 91 hence zero participants.

### Statistical analyses

No statistical analyses for this end point

## Primary: Number of participants with solicited local AEs after the vaccination with Placebo at Day 1

| End point title | Number of participants with solicited local AEs after the vaccination with Placebo at Day 1[15] |
|---|---|

End point description:

Solicited local adverse events assessed are injection site pain, erythema, swelling, induration. Any solicited local AEs = occurrence of the symptom regardless of intensity grade. Analysis was performed on ES population. Only participants with data available at specified timepoints were included in the analysis.

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

End point timeframe:

During 7 days after the Placebo vaccination at Day 1

Notes:

[15] - 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: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| End point values | MenB+MenACWY Group | MenB Group | MenACWY Group | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0[16] | 306 | 320 | |
| Units: Participants | | | | |
| Erythema | | 2 | 2 | |
| Induration | | 5 | 0 | |
| Pain | | 78 | 77 | |
| Swelling | | 2 | 1 | |

Notes:

[16] - Participants in this group did not receive Placebo on Day 1 hence zero participants.

### Statistical analyses

No statistical analyses for this end point

## Primary: Number of participants with solicited local AEs after the vaccination with Placebo at Day 91

| End point title | Number of participants with solicited local AEs after the vaccination with Placebo at Day 91[17] |
|---|---|

End point description:

Solicited local adverse events assessed are injection site pain, erythema, swelling, induration. Any solicited local AEs = occurrence of the symptom regardless of intensity grade. Analysis was performed on ES population. Only participants with data available at specified timepoints were included in the analysis. 1 participant in MenACWY Group received wrong study treatment at Day 91 (placebo instead of rMenB+OMV NZ), hence was considered in the analysis population.

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

End point timeframe:

During 7 days after the Placebo vaccination at Day 91

Notes:

[17] - 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: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| **End point values** | MenB+MenACWY Group | MenB Group | MenACWY Group | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 282 | 0[18] | 1 | |
| Units: Participants | | | | |
| Erythema | 1 | | 0 | |
| Induration | 1 | | 0 | |
| Pain | 25 | | 0 | |
| Swelling | 0 | | 0 | |

Notes:

[18] - Participants in this group did not receive Placebo on Day 91 hence zero participants.

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of participants with solicited systemic AEs at Day 1

| End point title | Number of participants with solicited systemic AEs at Day 1[19] |
|---|---|

End point description:

Solicited systemic adverse events assessed are fever [temperature >= 38.0°C], nausea, fatigue, myalgia, arthralgia, and headache. Analysis was performed on ES population. Only participants with data available at specified timepoints were included in the analysis.

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

End point timeframe:

During 7 days after the first study intervention administration occurring at Day 1

Notes:

[19] - 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: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| **End point values** | MenB+MenACWY Group | MenB Group | MenACWY Group | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 307 | 306 | 320 | |
| Units: Participants | | | | |
| Arthralgia | 24 | 32 | 24 | |
| Fatigue | 114 | 118 | 108 | |
| Headache | 128 | 135 | 134 | |
| Myalgia | 36 | 49 | 31 | |

| | | | | |
|---|---|---|---|---|
| Nausea | 46 | 57 | 51 | |
| Fever | 7 | 10 | 2 | |

### Statistical analyses

No statistical analyses for this end point

## Primary: Number of participants with solicited systemic AEs at Day 91

| End point title | Number of participants with solicited systemic AEs at Day 91[20] |
|---|---|

End point description:

Solicited systemic adverse events assessed are fever [temperature >= 38.0°C], nausea, fatigue, myalgia, arthralgia, and headache. Analysis was performed on ES population. Only participants with data available at specified timepoints were included in the analysis.

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

End point timeframe:

During 7 days after the third study intervention administration occurring at Day 91

Notes:

[20] - 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: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| End point values | MenB+MenACWY Group | MenB Group | MenACWY Group | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 282 | 263 | 270 | |
| Units: Participants | | | | |
| Arthralgia | 7 | 8 | 24 | |
| Fatigue | 38 | 59 | 86 | |
| Headache | 56 | 53 | 84 | |
| Myalgia | 7 | 16 | 39 | |
| Nausea | 20 | 18 | 31 | |
| Fever | 2 | 2 | 6 | |

### Statistical analyses

No statistical analyses for this end point

## Primary: Number of participants with solicited systemic AEs at Day 61

| End point title | Number of participants with solicited systemic AEs at Day 61[21] |
|---|---|

End point description:

Solicited systemic adverse events assessed are fever [temperature >= 38.0°C], nausea, fatigue, myalgia, arthralgia, and headache. Analysis was performed on ES population. Only participants with data available at specified timepoints were included in the analysis.

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

End point timeframe:

During 7 days after the second study intervention administration occurring at Day 61

Notes:

[21] - 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: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| **End point values** | MenB+MenACWY Group | MenB Group | MenACWY Group | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 284 | 269 | 287 | |
| Units: Participants | | | | |
| Arthralgia | 28 | 24 | 27 | |
| Fatigue | 96 | 101 | 88 | |
| Headache | 112 | 103 | 93 | |
| Myalgia | 41 | 42 | 43 | |
| Nausea | 37 | 37 | 40 | |
| Fever | 4 | 8 | 6 | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of participants with any unsolicited AEs (including all Serious Adverse Events) at Day 1

| End point title | Number of participants with any unsolicited AEs (including all Serious Adverse Events) at Day 1[22] |
|---|---|

End point description:

Unsolicited adverse events are defined as any AE reported in addition to those solicited during the clinical study. Also, any 'solicited' symptom with onset outside the specified period of follow-up for solicited symptoms are reported as an unsolicited adverse event. Any solicited AE that has not resolved within 30 days post vaccination and is reported during clinic visits or safety follow-up calls is entered into the subject's electronic Case Report Form (eCRF) as an unsolicited AE. Serious Adverse Events (SAEs) are any untoward medical occurrence that result in death, are life-threatening, require hospitalization or prolongation of existing hospitalization, result in disability/incapacity and is a congenital anomaly/birth defect in the offspring of a study subject. Analysis was performed on ES population. Only participants with data available at specified timepoints were included in the analysis.

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

End point timeframe:

During 30 days after the first study intervention administration occurring at Day 1

Notes:

[22] - 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: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| **End point values** | MenB+MenACWY Group | MenB Group | MenACWY Group | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 310 | 308 | 320 | |
| Units: Participants | 49 | 54 | 55 | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of participants with any unsolicited AEs (including all Serious Adverse Events) at Day 61

| End point title | Number of participants with any unsolicited AEs (including all Serious Adverse Events) at Day 61[23] |
|---|---|

End point description:

Unsolicited adverse events are defined as any AE reported in addition to those solicited during the clinical study. Also, any 'solicited' symptom with onset outside the specified period of follow-up for solicited symptoms are reported as an unsolicited adverse event. Any solicited AE that has not resolved within 30 days post vaccination and is reported during clinic visits or safety follow-up calls is entered into the subject's electronic Case Report Form (eCRF) as an unsolicited AE. Serious Adverse Events (SAEs) are any untoward medical occurrence that result in death, are life-threatening, require hospitalization or prolongation of existing hospitalization, result in disability/incapacity and is a congenital anomaly/birth defect in the offspring of a study subject. Analysis was performed on ES population. Only participants with data available at specified timepoints were included in the analysis.

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

End point timeframe:

During 30 days after the second study intervention administration occurring at Day 61

Notes:

[23] - 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: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| **End point values** | MenB+MenACWY Group | MenB Group | MenACWY Group | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 310 | 308 | 320 | |
| Units: Participants | 51 | 47 | 44 | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of participants with any unsolicited AEs (including all Serious Adverse Events) at Day 91

| End point title | Number of participants with any unsolicited AEs (including all Serious Adverse Events) at Day 91[24] |
|---|---|

End point description:

Unsolicited adverse events are defined as any AE reported in addition to those solicited during the clinical study. Also, any 'solicited' symptom with onset outside the specified period of follow-up for solicited symptoms are reported as an unsolicited adverse event. Any solicited AE that has not resolved within 30 days post vaccination and is reported during clinic visits or safety follow-up calls is entered into the subject's electronic Case Report Form (eCRF) as an unsolicited AE. Serious Adverse Events (SAEs) are any untoward medical occurrence that result in death, are life-threatening, require hospitalization or prolongation of existing hospitalization, result in disability/incapacity and is a congenital anomaly/birth defect in the offspring of a study subject. Analysis was performed on ES population. Only participants with data available at specified timepoints were included in the analysis.

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

End point timeframe:

During 30 days after the third study intervention administration occurring at Day 91

Notes:

[24] - 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: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| **End point values** | MenB+MenACWY Group | MenB Group | MenACWY Group | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 310 | 308 | 320 | |
| Units: Participants | 37 | 37 | 38 | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of participants with any AEs/SAEs leading to withdrawal at Day 61

| End point title | Number of participants with any AEs/SAEs leading to withdrawal at Day 61[25] |
|---|---|

End point description:

Unsolicited AEs are any AE reported beyond those solicited during the clinical study. A solicited symptom reported outside the designated follow-up period is considered an unsolicited AE. Any solicited AE that has not resolved within 30 days post vaccination and is reported during clinic visits/safety follow-up calls is entered into the subject's eCRF as an unsolicited AE. SAEs are any untoward medical occurrence that result in death, are life-threatening, require hospitalization/prolongation of existing hospitalization, result in disability/incapacity and is a congenital anomaly/birth defect in the offspring of a study subject. A participant was considered a 'withdrawal' from study when no study procedure has occurred, no follow-up has been performed and no further information has been collected for this participant from the date of withdrawal/last contact. Analysis was performed on ES population,participants with data available at specified timepoints were included in the analysis.

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

End point timeframe:

During 30 days after the second study intervention administration occurring at Day 61

Notes:

[25] - 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: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| **End point values** | MenB+MenACWY Group | MenB Group | MenACWY Group | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 310 | 308 | 320 | |
| Units: Participants | 0 | 0 | 0 | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of participants with any AEs/SAEs leading to withdrawal at Day 1

| End point title | Number of participants with any AEs/SAEs leading to withdrawal at Day 1[26] |
|---|---|

End point description:

Unsolicited AEs are any AE reported beyond those solicited during the clinical study. A solicited symptom reported outside the designated follow-up period is considered an unsolicited AE. Any solicited AE that has not resolved within 30 days post vaccination and is reported during clinic visits/safety follow-up calls is entered into the subject's eCRF as an unsolicited AE. SAEs are any untoward medical occurrence that result in death, are life-threatening, require hospitalization/prolongation of existing hospitalization, result in disability/incapacity and is a congenital anomaly/birth defect in the offspring of a study subject. A participant was considered a 'withdrawal' from study when no study procedure has occurred, no follow-up has been performed and no further information has been collected for this participant from the date of withdrawal/last contact. Analysis was performed on ES population,participants with data available at specified timepoints were included in the analysis.

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

End point timeframe:

During 30 days after the first study intervention administration occurring at Day 1

Notes:

[26] - 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: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| **End point values** | MenB+MenACWY Group | MenB Group | MenACWY Group | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 310 | 308 | 320 | |
| Units: Participants | 0 | 0 | 1 | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of participants with any AEs/SAEs leading to withdrawal at Day 91

| End point title | Number of participants with any AEs/SAEs leading to withdrawal at Day 91[27] |
|---|---|

End point description:

Unsolicited AEs are any AE reported beyond those solicited during the clinical study. A solicited symptom reported outside the designated follow-up period is considered an unsolicited AE. Any solicited AE that has not resolved within 30 days post vaccination and is reported during clinic visits/safety follow-up calls is entered into the subject's eCRF as an unsolicited AE. SAEs are any untoward medical occurrence that result in death, are life-threatening, require hospitalization/prolongation of existing hospitalization, result in disability/incapacity and is a congenital anomaly/birth defect in the offspring of a study subject. A participant was considered a 'withdrawal' from study when no study procedure has occurred, no follow-up has been performed and no further information has been collected for this participant from the date of withdrawal/last contact. Analysis was performed on ES population,participants with data available at specified timepoints were included in the analysis.

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

End point timeframe:

During 30 days after the third study intervention administration occurring at Day 91

Notes:

[27] - 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: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| End point values | MenB+MenACWY Group | MenB Group | MenACWY Group | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 310 | 308 | 320 | |
| Units: Participants | 0 | 0 | 0 | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of participants with any medically attended AEs at Day 61

| End point title | Number of participants with any medically attended AEs at Day 61[28] |
|---|---|

End point description:

Medically attended AEs are symptoms or illnesses requiring hospitalization, or emergency room visit, or visit to/by a health care provider. Analysis was performed on ES population. Only participants with data available at specified timepoints were included in the analysis.

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

End point timeframe:

During 30 days after the second study intervention administration occurring at Day 61

Notes:

[28] - 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: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| End point values | MenB+MenACWY Group | MenB Group | MenACWY Group | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 310 | 308 | 320 | |
| Units: Participants | 28 | 32 | 25 | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of participants with any medically attended AEs at Day 1

| End point title | Number of participants with any medically attended AEs at Day 1[29] |
|---|---|

End point description:

Medically attended AEs are symptoms or illnesses requiring hospitalization, or emergency room visit, or visit to/by a health care provider. Analysis was performed on ES population. Only participants with data available at specified timepoints were included in the analysis.

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

End point timeframe:

During 30 days after the first study intervention administration occurring at Day 1

Notes:

[29] - 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: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| End point values | MenB+MenACWY Group | MenB Group | MenACWY Group | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 310 | 308 | 320 | |
| Units: Participants | 28 | 36 | 26 | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of participants with any SAEs, AEs leading to withdrawal and medically attended AEs

| End point title | Number of participants with any SAEs, AEs leading to withdrawal and medically attended AEs[30] |
|---|---|

End point description:

SAEs, AEs leading to withdrawal and medically attended AEs were assessed throughout the study period and are reported in this outcome measure. Analysis was performed on the ES population, which included all participants who received at least one dose of the study treatment. Allocation per group is based on the treatment administered.

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

End point timeframe:

Throughout the study period (Day 1 to Day 271)

Notes:

[30] - 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: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| End point values | MenB+MenACWY Group | MenB Group | MenACWY Group | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 310 | 308 | 320 | |
| Units: Participants | | | | |
| SAEs | 2 | 3 | 5 | |
| AEs leading to withdrawal | 0 | 0 | 1 | |
| Medically attended AEs | 93 | 103 | 96 | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of participants with any medically attended AEs at Day 91

| End point title | Number of participants with any medically attended AEs at Day 91[31] |
|---|---|

End point description:

Medically attended AEs are symptoms or illnesses requiring hospitalization, or emergency room visit, or visit to/by a health care provider. Analysis was performed on ES population. Only participants with data available at specified timepoints were included in the analysis.

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

End point timeframe:

During 30 days after the third study intervention administration occurring at Day 91

Notes:

[31] - 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: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| **End point values** | MenB+MenACWY Group | MenB Group | MenACWY Group | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 310 | 308 | 320 | |
| Units: Participants | 19 | 21 | 17 | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of participants who received rMenB+OMV NZ with adverse events of special interest (AESI)

| End point title | Number of participants who received rMenB+OMV NZ with adverse events of special interest (AESI)[32] |
|---|---|

End point description:

AESIs are predefined (serious or non-serious) adverse events of scientific and medical concern specific to the product or program, for which ongoing monitoring and rapid communication by the investigator to the sponsor can be appropriate, because such an event might warrant further investigation in order to characterize and understand it. Analysis was performed on ES population. Only participants with data available at specified timepoints were included in the analysis.

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

End point timeframe:

Throughout the study period (Day 1 to Day 271)

Notes:

[32] - 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: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| **End point values** | MenB+MenACWY Group | MenB Group | MenACWY Group | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 310 | 308 | 320 | |
| Units: Participants | 0 | 0 | 0 | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of participants who received rMenB+OMV NZ with AESI

| End point title | Number of participants who received rMenB+OMV NZ with AESI[33] |
|---|---|

End point description:

AESIs are predefined (serious or non-serious) adverse events of scientific and medical concern specific to the product or program, for which ongoing monitoring and rapid communication by the investigator to the sponsor can be appropriate, because such an event might warrant further investigation in order to characterize and understand it. Analysis was performed on ES population. Only participants with data available at specified timepoints (during safety follow-up period from Day 271 to Day 451) were included in the analysis.

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

End point timeframe:

During safety follow-up (Day 271 to Day 451)

Notes:

[33] - 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: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| **End point values** | MenB+MenACWY Group | MenB Group | MenACWY Group | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 88 | 90 | 87 | |
| Units: Participants | 0 | 0 | 0 | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of participants with any SAEs and AEs leading to withdrawal

| End point title | Number of participants with any SAEs and AEs leading to withdrawal[34] |
|---|---|

End point description:

Unsolicited AEs are any AE reported beyond those solicited during the clinical study. A solicited symptom reported outside the designated follow-up period is considered an unsolicited AE. Any solicited AE that has not resolved within 30 days post vaccination and is reported during clinic visits/safety follow-up calls is entered into the subject's eCRF as an unsolicited AE. SAEs are any untoward medical occurrence that result in death, are life-threatening, require hospitalization or prolongation, causing disability/incapacity and is a congenital anomaly/birth defect in the offspring of study subject. A participant is considered a 'withdrawal' from the study if no further study procedures, follow-ups, or data collection have occurred since the withdrawal/last contact date. Analysis was performed on ES population,participants with data available at specified timepoints (during safety follow-up period from Day 271 to Day 451) were included in the analysis.

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

End point timeframe:

During safety follow-up (Day 271 to Day 451)

Notes:

[34] - 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: The analysis of this primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

| **End point values** | MenB+MenACWY Group | MenB Group | MenACWY Group | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 88 | 90 | 87 | |
| Units: Participants | | | | |
| SAEs | 0 | 1 | 2 | |
| AEs leading to withdrawal | 0 | 0 | 0 | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Human Serum Bactericidal Assay (hSBA) Geometric Mean Titers (GMTs) against each of the N. meningitidis serogroup B strains at 1 month after the second vaccination with rMenB+OMV NZ (groups MenB+MenACWY and MenB), and between-group GMT ratios

| End point title | Human Serum Bactericidal Assay (hSBA) Geometric Mean Titers (GMTs) against each of the N. meningitidis serogroup B strains at 1 month after the second vaccination with rMenB+OMV NZ (groups MenB+MenACWY and MenB), and between-group GMT ratios[35] |
|---|---|

End point description:

hSBA titers were measured by serum bactericidal assay and expressed as Geometric Mean Titers (GMTs) against N. meningitidis serogroup B indicator strains (M14459 [fHbp], 96217 [NadA], NZ98/254 [PorA] and M13520 [NHBA]). Analysis was performed on the Per Protocol Set (PPS), which included participants who received at least 1 dose of the study intervention to which they were randomized and had post-vaccination data available at the specified timepoint minus participants with protocol deviations that led to exclusion from the PPS.

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

End point timeframe:

At Day 91 (1 month after the second vaccination with rMenB+OMV NZ in MenB+MenACWY and MenB groups)

Notes:

[35] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: As specified in the Protocol, the analysis assess the imqmune response to rMenB+OMV NZ in healthy subjects 16-18 years of age against N. meningitidis serogroup B test strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA) and M07-0241084 (NHBA), at one month after the second vaccination with rMenB+OMV NZ.

| **End point values** | MenB+MenACWY Group | MenB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 274 | 267 | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| fHbp (M14459) | 16.9 (14.4 to 19.8) | 18.7 (15.9 to 21.9) | | |
| NadA (96217) | 239.6 (202.9 to 283.0) | 272.4 (231.1 to 321.0) | | |
| PorA (NZ98/254) | 18.8 (15.6 to 22.6) | 21.3 (17.7 to 25.6) | | |
| NHBA (M13520) | 19.0 (15.6 to 23.1) | 20.5 (16.9 to 24.9) | | |

## Statistical analyses

| Statistical analysis title | Statistical Analysis 1 |
|---|---|

Statistical analysis description:

To demonstrate the non-inferiority (NI) of the antibody response to rMenB+OMV NZ given concomitantly with MenACWY compared to rMenB+OMV NZ administered alone, measured by hSBA GMTs against N. meningitidis serogroup B indicator strains at one month after the second vaccination with rMenB+OMV NZ (at Day 91).

| | |
|---|---|
| Comparison groups | MenB Group v MenB+MenACWY Group |
| Number of subjects included in analysis | 541 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | ANOVA |
| Parameter estimate | GMT Ratio |
| Point estimate | 0.9 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.77 |
| upper limit | 1.06 |

| Statistical analysis title | Statistical Analysis 2 |
|---|---|

Statistical analysis description:

To demonstrate the non-inferiority of the antibody response to rMenB+OMV NZ given concomitantly with MenACWY compared to rMenB+OMV NZ administered alone, measured by hSBA GMTs against N. meningitidis serogroup B indicator strains at one month after the second vaccination with rMenB+OMV NZ (at Day 91).

| | |
|---|---|
| Comparison groups | MenB+MenACWY Group v MenB Group |
| Number of subjects included in analysis | 541 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | ANOVA |
| Parameter estimate | GMT Ratio |
| Point estimate | 0.88 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.75 |
| upper limit | 1.04 |

| Statistical analysis title | Statistical Analysis 3 |
|---|---|

Statistical analysis description:

To demonstrate the non-inferiority of the antibody response to rMenB+OMV NZ given concomitantly with MenACWY compared to rMenB+OMV NZ administered alone, measured by hSBA GMTs against N. meningitidis serogroup B indicator strains at one month after the second vaccination with rMenB+OMV NZ (at Day 91).

| | |
|---|---|
| Comparison groups | MenB+MenACWY Group v MenB Group |

| | |
|---|---|
| Number of subjects included in analysis | 541 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | ANOVA |
| Parameter estimate | GMT Ratio |
| Point estimate | 0.93 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.76 |
| upper limit | 1.12 |

| **Statistical analysis title** | Statistical Analysis 4 |
|---|---|

Statistical analysis description:

To demonstrate the non-inferiority of the antibody response to rMenB+OMV NZ given concomitantly with MenACWY compared to rMenB+OMV NZ administered alone, measured by hSBA GMTs against N. meningitidis serogroup B indicator strains at one month after the second vaccination with rMenB+OMV NZ (at Day 91).

| | |
|---|---|
| Comparison groups | MenB+MenACWY Group v MenB Group |
| Number of subjects included in analysis | 541 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | ANOVA |
| Parameter estimate | GMT Ratio |
| Point estimate | 0.88 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.73 |
| upper limit | 1.06 |

## Primary: hSBA GMTs against each of the N. meningitidis serogroups A, C, W and Y after vaccination with MenACWY (groups MenB+MenACWY and MenACWY), and between-group GMT ratios

| | |
|---|---|
| End point title | hSBA GMTs against each of the N. meningitidis serogroups A, C, W and Y after vaccination with MenACWY (groups MenB+MenACWY and MenACWY), and between-group GMT ratios[36] |

End point description:

hSBA titers were measured by serum bactericidal assay and expressed as GMTs against each of the 4 serogroups Men A, Men C, Men W and Men Y. Analysis was performed on PPS population. Only those participants with data available at specified timepoint were included in analysis.

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

End point timeframe:

At Day 31 (1 month after the vaccination with MenACWY in MenACWY and MenB+MenACWY groups)

Notes:

[36] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As specified in the Protocol, the analysis assess the immune response to MenACWY in

healthy subjects 16-18 years of age against each of the serogroups A, C, W and Y, at one month after the (study) vaccination with MenACWY.

| End point values | MenB+MenACWY Group | MenACWY Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 295 | 303 | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Men A | 2388.8 (1977.2 to 2886.1) | 2536.1 (2095.7 to 3069.1) | | |
| Men C | 2075.9 (1602.5 to 2689.3) | 1867.6 (1438.7 to 2424.2) | | |
| Men W | 2299.3 (1902.5 to 2778.9) | 2305.7 (1905.3 to 2790.4) | | |
| Men Y | 2897.3 (2359.2 to 3558.3) | 2802.0 (2278.3 to 3446.2) | | |

**Statistical analyses**

| Statistical analysis title | Statistical Analysis 1 |
|---|---|

Statistical analysis description:

To demonstrate the non-inferiority of the antibody response to MenACWY given concomitantly with rMenB+OMV NZ compared to MenACWY administered alone, as measured by hSBA GMTs against the N. meningitidis serogroup Men A, at one month after the vaccination with MenACWY (at Day 31).

| | |
|---|---|
| Comparison groups | MenB+MenACWY Group v MenACWY Group |
| Number of subjects included in analysis | 598 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | ANOVA |
| Parameter estimate | GMT Ratio |
| Point estimate | 0.94 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.78 |
| upper limit | 1.14 |

| Statistical analysis title | Statistical Analysis 4 |
|---|---|

Statistical analysis description:

To demonstrate the non-inferiority of the antibody response to MenACWY given concomitantly with rMenB+OMV NZ compared to MenACWY administered alone, as measured by hSBA GMTs against the N. meningitidis serogroup Men Y, at one month after the vaccination with MenACWY (at Day 31).

| | |
|---|---|
| Comparison groups | MenB+MenACWY Group v MenACWY Group |

| | |
|---|---|
| Number of subjects included in analysis | 598 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | ANOVA |
| Parameter estimate | GMT Ratio |
| Point estimate | 1.03 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.84 |
| upper limit | 1.27 |

| **Statistical analysis title** | Statistical Analysis 3 |
|---|---|

Statistical analysis description:

To demonstrate the non-inferiority of the antibody response to MenACWY given concomitantly with rMenB+OMV NZ compared to MenACWY administered alone, as measured by hSBA GMTs against the N. meningitidis serogroup Men W, at one month after the vaccination with MenACWY (at Day 31).

| | |
|---|---|
| Comparison groups | MenB+MenACWY Group v MenACWY Group |
| Number of subjects included in analysis | 598 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | ANOVA |
| Parameter estimate | GMT Ratio |
| Point estimate | 1 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.82 |
| upper limit | 1.21 |

| **Statistical analysis title** | Statistical Analysis 2 |
|---|---|

Statistical analysis description:

To demonstrate the non-inferiority of the antibody response to MenACWY given concomitantly with rMenB+OMV NZ compared to MenACWY administered alone, as measured by hSBA GMTs against the N. meningitidis serogroup Men C, at one month after the vaccination with MenACWY (at Day 31).

| | |
|---|---|
| Comparison groups | MenB+MenACWY Group v MenACWY Group |
| Number of subjects included in analysis | 598 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | ANOVA |
| Parameter estimate | GMT Ratio |
| Point estimate | 1.11 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.86 |
| upper limit | 1.44 |

## Secondary: hSBA Geometric Mean Concentrations (GMCs) measured by ECL against each of the N. meningitidis serogroups after MenACWY vaccination

| End point title | hSBA Geometric Mean Concentrations (GMCs) measured by ECL against each of the N. meningitidis serogroups after MenACWY vaccination |
|---|---|

End point description:

Immune response to MenACWY given with or without rMenB+OMV NZ, as measured by lectrochemiluminescence-based multiplex (ECL) GMCs against each of the serogroups A, C, W and Y. ECL (validated assay) was used because ELISA is not validated. Analysis was performed on the PPS population, which included participants who received at least 1 dose of the study intervention to which they were randomized and had post-vaccination data available at the specified timepoint minus participants with protocol deviations that led to exclusion from the PPS. 99999" is used as a placeholder value for the results for all the groups since the analysis of final results for these groups is ongoing and will be updated subsequently.

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

End point timeframe:

At Day 31 (1 month after the vaccination of MenACWY in MenACWY and MenB+MenACWY groups)

| **End point values** | MenB+MenACWY Group | MenB Group | MenACWY Group | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 310 | 308 | 320 | |
| Units: IU/L | | | | |
| geometric mean (confidence interval 95%) | 99999 (99999 to 99999) | 99999 (99999 to 99999) | 99999 (99999 to 99999) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: hSBA GMTs against each of the serogroup B strains in both MenB+MenACWY and MenB Groups after first rMenB+OMV NZ vaccination and between-group GMT ratios

| End point title | hSBA GMTs against each of the serogroup B strains in both MenB+MenACWY and MenB Groups after first rMenB+OMV NZ vaccination and between-group GMT ratios[37] |
|---|---|

End point description:

hSBA titers were measured by bactericidal activity against N. meningitidis serogroup B indicator strains (M14459 [fHbp], 96217 [NadA], NZ98/254 [PorA] and M13520 [NHBA]) and expressed in GMTs. Analysis was performed on PPS population. Only those participants with data available at specified timepoint were included in analysis.

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

End point timeframe:

At Day 31 (1 month after first vaccination with rMenB+OMV NZ)

Notes:

[37] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As specified in the Protocol, the analysis assess the imqmune response to rMenB+OMV NZ

in healthy subjects 16-18 years of age against N. meningitidis serogroup B test strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA) and M07-0241084 (NHBA), at one month after the first vaccination with rMenB+OMV NZ.

| **End point values** | MenB+MenACWY Group | MenB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 294 | 294 | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| fHbp (M14459) | 4.3 (3.6 to 5.1) | 5.6 (4.7 to 6.7) | | |
| NadA (96217) | 45.2 (36.0 to 56.9) | 73.4 (58.5 to 91.9) | | |
| PorA (NZ98/254) | 4.2 (3.5 to 5.0) | 5.6 (4.7 to 6.6) | | |
| NHBA (M13520) | 6.4 (5.1 to 8.1) | 8.8 (7.0 to 11.1) | | |

## Statistical analyses

| **Statistical analysis title** | Statistical Analysis 1 |
|---|---|

Statistical analysis description:

To assess the immune response to rMenB+OMV NZ given concomitantly with MenACWY compared to rMenB+OMV NZ administered alone, measured by hSBA GMTs against N. meningitidis M14459 (fHbp) strain at one month after the first vaccination with rMenB+OMV NZ (at Day 31).

| | |
|---|---|
| Comparison groups | MenB+MenACWY Group v MenB Group |
| Number of subjects included in analysis | 588 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | ANOVA |
| Parameter estimate | GMT Ratio |
| Point estimate | 0.76 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.64 |
| upper limit | 0.91 |

| **Statistical analysis title** | Statistical Analysis 2 |
|---|---|

Statistical analysis description:

To assess the immune response to rMenB+OMV NZ given concomitantly with MenACWY compared to rMenB+OMV NZ administered alone, measured by hSBA GMTs against N. meningitidis 96217 (NadA) strain at one month after the first vaccination with rMenB+OMV NZ (at Day 31).

| | |
|---|---|
| Comparison groups | MenB+MenACWY Group v MenB Group |

| | |
|---|---|
| Number of subjects included in analysis | 588 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | ANOVA |
| Parameter estimate | GMT Ratio |
| Point estimate | 0.62 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.49 |
| upper limit | 0.77 |

| **Statistical analysis title** | Statistical Analysis 3 |
|---|---|

Statistical analysis description:

To assess the immune response to rMenB+OMV NZ given concomitantly with MenACWY compared to rMenB+OMV NZ administered alone, measured by hSBA GMTs against N. meningitidis NZ98/254 (PorA) strain at one month after the first vaccination with rMenB+OMV NZ (at Day 31).

| | |
|---|---|
| Comparison groups | MenB+MenACWY Group v MenB Group |
| Number of subjects included in analysis | 588 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | ANOVA |
| Parameter estimate | GMT Ratio |
| Point estimate | 0.73 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.58 |
| upper limit | 0.91 |

| **Statistical analysis title** | Statistical Analysis 4 |
|---|---|

Statistical analysis description:

To assess the immune response to rMenB+OMV NZ given concomitantly with MenACWY compared to rMenB+OMV NZ administered alone, measured by hSBA GMTs against N. meningitidis M13520 (NHBA) at one month after the first vaccination with rMenB+OMV NZ (at Day 31).

| | |
|---|---|
| Comparison groups | MenB+MenACWY Group v MenB Group |
| Number of subjects included in analysis | 588 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | ANOVA |
| Parameter estimate | GMT Ratio |
| Point estimate | 0.76 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.64 |
| upper limit | 0.9 |

## Secondary: GMRs against each of the N. meningitidis serogroup B strains in both MenB+MenACWY and MenB Groups after the second rMenB+OMV NZ vaccination

| End point title | GMRs against each of the N. meningitidis serogroup B strains in both MenB+MenACWY and MenB Groups after the second rMenB+OMV NZ vaccination[38] |
|---|---|

End point description:

The immune response to rMenB+OMV NZ was measured by bactericidal activity against N. meningitidis serogroup B indicator strains (M14459 [fHbp], 96217 [NadA], NZ98/254 [PorA] and M13520 [NHBA]) in terms of GMRs (after vaccination/baseline). Analysis was performed on PPS population. Only those participants with data available at specified timepoint were included in analysis.

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

End point timeframe:

At Day 91 (1 month after the second rMenB+OMV NZ vaccination) compared to the baseline (Day 1)

Notes:

[38] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As specified in the Protocol, the analysis assess the imqmune response to rMenB+OMV NZ in healthy subjects 16-18 years of age against N. meningitidis serogroup B test strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA) and M07-0241084 (NHBA), at one month after the second vaccination with rMenB+OMV NZ.

| End point values | MenB+MenACWY Group | MenB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 274 | 267 | | |
| Units: Ratio | | | | |
| geometric mean (confidence interval 95%) | | | | |
| fHbp (M14459) | 6.4 (5.5 to 7.5) | 7.0 (5.9 to 8.1) | | |
| NadA (96217) | 30.7 (25.8 to 36.6) | 35.1 (29.5 to 41.7) | | |
| PorA (NZ98/254) | 6.0 (5.0 to 7.2) | 6.9 (5.8 to 8.3) | | |
| NHBA (M13520) | 5.2 (4.4 to 6.2) | 5.6 (4.7 to 6.6) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Geometric mean ratios (GMRs) against each of the N. meningitidis serogroup B strains in both MenB+MenACWY and MenB Groups after the first rMenB+OMV NZ vaccination

| End point title | Geometric mean ratios (GMRs) against each of the N. meningitidis serogroup B strains in both MenB+MenACWY and MenB Groups after the first rMenB+OMV NZ vaccination[39] |
|---|---|

End point description:

The immune response to rMenB+OMV NZ was measured by bactericidal activity against N. meningitidis serogroup B indicator strains (M14459 [fHbp], 96217 [NadA], NZ98/254 [PorA] and M13520 [NHBA]) in terms of GMRs (after vaccination/baseline). Analysis was performed on PPS population. Only those participants with data available at specified timepoint were included in analysis.

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

End point timeframe:

At Day 31 (1 month after first rMenB+OMV NZ vaccination) compared to the baseline (Day 1)

Notes:

[39] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As specified in the Protocol, the analysis assess the immune response to rMenB+OMV NZ in healthy subjects 16-18 years of age against N. meningitidis serogroup B test strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA) and M07-0241084 (NHBA), at one month after the first vaccination with rMenB+OMV NZ.

| **End point values** | MenB+MenACWY Group | MenB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 294 | 294 | | |
| Units: Ratio | | | | |
| geometric mean (confidence interval 95%) | | | | |
| fHbp (M14459) | 1.6 (1.4 to 1.9) | 2.0 (1.7 to 2.4) | | |
| NadA (96217) | 5.9 (4.7 to 7.4) | 9.3 (7.5 to 11.6) | | |
| PorA (NZ98/254) | 1.4 (1.2 to 1.6) | 1.8 (1.5 to 2.1) | | |
| NHBA (M13520) | 1.8 (1.5 to 2.2) | 2.3 (1.9 to 2.8) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of participants with hSBA titers >= lower limit of quantitation (LLOQ) for each and all serogroup B test strains in both MenB+MenACWY and MenB Groups after the first rMenB+OMV NZ vaccination

| End point title | Percentage of participants with hSBA titers >= lower limit of quantitation (LLOQ) for each and all serogroup B test strains in both MenB+MenACWY and MenB Groups after the first rMenB+OMV NZ vaccination[40] |
|---|---|

End point description:

The immune response to rMenB+OMV NZ vaccine is evaluated by measuring bactericidal activity in terms of participants with hSBA titers >= LLOQ against N. meningitidis serogroup B test strains (M14459 [fHbp], 96217 [NadA], NZ98/254 [PorA] and M13520 [NHBA]). Analysis was performed on PPS population. Only those participants with data available at specified timepoint were included in analysis.

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

End point timeframe:

At Day 31 (one month after the first rMenB+OMV NZ vaccination)

Notes:

[40] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As specified in the Protocol, the analysis assess the imqmune response to rMenB+OMV NZ in healthy subjects 16-18 years of age against N. meningitidis serogroup B test strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA) and M07-0241084 (NHBA), at one month after the first vaccination with rMenB+OMV NZ.

| End point values | MenB+MenACWY Group | MenB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 294 | 294 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| fHbp (M14459) | 32.3 (27.0 to 38.0) | 44.9 (39.1 to 50.8) | | |
| NadA (96217) | 77.9 (72.7 to 82.5) | 85.7 (81.2 to 89.5) | | |
| PorA ( NZ98/254) | 21.1 (16.6 to 26.2) | 30.4 (25.2 to 36.0) | | |
| NHBA (M13520) | 37.1 (31.5 to 42.9) | 44.4 (38.6 to 50.3) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of participants with hSBA titers >= LLOQ for each and all of the serogroup B test strains in both MenB+MenACWY and MenB Groups after the second rMenB+OMV NZ vaccination

| End point title | Percentage of participants with hSBA titers >= LLOQ for each and all of the serogroup B test strains in both MenB+MenACWY and MenB Groups after the second rMenB+OMV NZ vaccination[41] |
|---|---|

End point description:

The immune response to rMenB+OMV NZ vaccine is evaluated by measuring bactericidal activity in terms of participants with hSBA titers >= LLOQ against N. meningitidis serogroup B test strains (M14459 [fHbp], 96217 [NadA], NZ98/254 [PorA] and M13520 [NHBA]). Analysis was performed on PPS population. Only those participants with data available at specified timepoint were included in analysis.

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

End point timeframe:

At Day 91 (1 month after the second rMenB+OMV NZ vaccination)

Notes:

[41] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As specified in the Protocol, the analysis assess the imqmune response to rMenB+OMV NZ in healthy subjects 16-18 years of age against N. meningitidis serogroup B test strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA) and M07-0241084 (NHBA), at one month after the second vaccination with rMenB+OMV NZ.

| End point values | MenB+MenACWY Group | MenB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 274 | 267 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| fHbp (M14459 ) | 92.3 (88.5 to 95.2) | 92.5 (88.6 to 95.3) | | |
| NadA (96217) | 99.6 (98.0 to 100) | 99.6 (97.9 to 100) | | |
| PorA (NZ98/254) | 83.2 (78.2 to 87.4) | 85.0 (80.1 to 89.0) | | |

| | | | | |
|---|---|---|---|---|
| NHBA (M13520) | 84.2 (79.4 to 88.4) | 90.2 (86.0 to 93.5) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of participants with 4-fold increase in hSBA titers relative to baseline in both MenB+MenACWY and MenB Groups after the first rMenB+OMV NZ vaccination

| End point title | Percentage of participants with 4-fold increase in hSBA titers relative to baseline in both MenB+MenACWY and MenB Groups after the first rMenB+OMV NZ vaccination[42] |
|---|---|

End point description:

The immune response to rMenB+OMV NZ vaccine is evaluated by measuring bactericidal activity against each of N. meningitidis serogroup B test strains (M14459 [fHbp], 96217 [NadA], NZ98/254 [PorA] and M13520 [NHBA]) in terms of the Four-fold increase defined as: - For a pre-vaccination titer < limit of detection (LOD), a post-vaccination titer of >= 4-fold the LOD or >= LLOQ, whichever is greater, - For a pre-vaccination titer >= LOD but <LLOQ, a post vaccination titer of at least 4-fold the LLOQ, - For a pre-vaccination titer >= LLOQ, a post vaccination titer of at least 4-fold the pre-vaccination titer. Analysis was performed on PPS population. Only those participants with data available at specified timepoint were included in analysis.

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

End point timeframe:

At 1 month after the first rMenB+OMV NZ vaccination (i.e at Day 31) relative to baseline (i.e. Day 1)

Notes:

[42] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As specified in the Protocol, the analysis assess the imqmune response to rMenB+OMV NZ in healthy subjects 16-18 years of age against N. meningitidis serogroup B test strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA) and M07-0241084 (NHBA), at one month after the first vaccination with rMenB+OMV NZ.

| **End point values** | MenB+MenACWY Group | MenB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 293 | 293 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| fHbp (M14459) | 14.7 (10.8 to 19.3) | 21.0 (16.4 to 26.1) | | |
| NadA (96217) | 68.9 (63.3 to 74.2) | 78.4 (73.3 to 83.0) | | |
| PorA (NZ98/254) | 8.9 (5.9 to 12.7) | 16.4 (12.4 to 21.2) | | |
| NHBA (M13520) | 17.4 (13.2 to 22.2) | 25.3 (20.4 to 30.6) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of participants with hSBA titers >=LLOQ for each of the serogroup A, C, W and Y in both MenB+MenACWY and MenACWY Groups after MenACWY vaccination

| End point title | Percentage of participants with hSBA titers >=LLOQ for each of the serogroup A, C, W and Y in both MenB+MenACWY and MenACWY Groups after MenACWY vaccination[43] |
|---|---|

End point description:

The immune response to MenACWY vaccines is expressed in terms of percentage of participants with hSBA titers >=LLOQ for each of the serogroup Men A, Men C, Men W and Men Y. Analysis was performed on PPS population. Only those participants with data available at specified timepoint were included in analysis.

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

End point timeframe:

At baseline (Day 1) and at one month after the MenACWY vaccination (i.e. Day 31)

Notes:

[43] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As specified in the Protocol, the analysis assesses the immune response to MenACWY in healthy subjects 16-18 years of age against each of the serogroups A, C, W and Y, at one month after the (study) vaccination with MenACWY.

| End point values | MenB+MenACWY Group | MenACWY Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 295 | 303 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Men A, Baseline (Day 1) | 28.1 (22.8 to 33.9) | 30.0 (24.7 to 35.9) | | |
| Men A, Day 31 | 99.7 (98.1 to 100) | 99.3 (97.5 to 99.9) | | |
| Men C, Baseline (Day 1) | 46.3 (40.5 to 52.1) | 44.4 (38.7 to 50.3) | | |
| Men C, Day 31 | 99.0 (97.1 to 99.8) | 98.7 (96.6 to 99.6) | | |
| Men W, Baseline (Day 1) | 27.4 (22.4 to 32.9) | 28.4 (23.3 to 34.0) | | |
| Men W, Day 31 | 100 (98.8 to 100) | 100 (98.8 to 100) | | |
| Men Y, Baseline (Day 1) | 23.4 (18.6 to 28.7) | 23.0 (18.3 to 28.2) | | |
| Men Y, Day 31 | 99.7 (98.1 to 100) | 99.7 (98.2 to 100) | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: GMRs against each of the N. meningitidis serogroup Men A, Men C, Men W and Men Y in both MenB+MenACWY and MenACWY Groups after MenACWY vaccination

| End point title | GMRs against each of the N. meningitidis serogroup Men A, |
|---|---|

| | |
|---|---|
| | Men C, Men W and Men Y in both MenB+MenACWY and MenACWY Groups after MenACWY vaccination[44] |

End point description:

Immune response to MenACWY given with or without rMenB+OMV NZ was measured by bactericidal activity against the four serogroups Men A, Men C, Men W and Men Y in terms of GMRs at one month after MenACWY vaccination compared to the baseline at Day 1/Month 0. GMR was measured within-group. Analysis was performed on PPS population. Only those participants with data available at specified timepoint were included in analysis.

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

End point timeframe:

At 1 month after MenACWY vaccination (i.e.at Day 31) compared to the baseline (Day 1)

Notes:

[44] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As specified in the Protocol, the analysis assesses the immune response to MenACWY in healthy subjects 16-18 years of age against each of the serogroups A, C, W and Y, at one month after the (study) vaccination with MenACWY.

| **End point values** | MenB+MenACWY Group | MenACWY Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 295 | 303 | | |
| Units: Ratio | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Men A | 150.2 (120.1 to 187.8) | 145.0 (115.4 to 182.2) | | |
| Men C | 130.0 (97.7 to 173.1) | 131.9 (98.8 to 176.1) | | |
| Men W | 294.2 (229.0 to 378.1) | 279.3 (216.6 to 360.1) | | |
| Men Y | 324.3 (252.2 to 417.0) | 300.0 (232.9 to 386.4) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of participants with 4-fold increase in hSBA titers relative to baseline in both MenB+MenACWY and MenB Groups after the second rMenB+OMV NZ vaccination

| End point title | Percentage of participants with 4-fold increase in hSBA titers relative to baseline in both MenB+MenACWY and MenB Groups after the second rMenB+OMV NZ vaccination[45] |
|---|---|

End point description:

The immune response to rMenB+OMV NZ vaccine is evaluated by measuring bactericidal activity against each of the N. meningitidis serogroup B test strains (M14459 [fHbp], 96217 [NadA], NZ98/254 [PorA] and M13520 [NHBA]) in terms of the Four-fold increase defined as: - For a pre-vaccination titer <LOD, a post-vaccination titer of >= 4-fold the LOD or >= LLOQ, whichever is greater, - For a pre-vaccination titer >=LOD but <LLOQ, a post vaccination titer of at least 4-fold the LLOQ, - For a pre-vaccination titer >=LLOQ, a post vaccination titer of at least 4-fold the pre-vaccination titer. Analysis was performed on PPS population. Only those participants with data available at specified timepoint were included in analysis.

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

End point timeframe:

At 1 month after the second rMenB+OMV vaccination (i.e at Day 91) relative to baseline (i.e. Day 1)

Notes:

[45] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As specified in the Protocol, the analysis assess the imqmune response to rMenB+OMV NZ in healthy subjects 16-18 years of age against N. meningitidis serogroup B test strains M14459 (fHbp), 96217 (NadA), NZ98/254 (PorA) and M07-0241084 (NHBA), at one month after the second vaccination with rMenB+OMV NZ.

| **End point values** | MenB+MenACWY Group | MenB Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 273 | 266 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| fHbp (M14459) | 57.1 (51.0 to 63.1) | 64.6 (58.5 to 70.4) | | |
| NadA (96217) | 96.0 (92.9 to 98.0) | 98.9 (96.7 to 99.8) | | |
| PorA (NZ98/254) | 51.5 (45.4 to 57.5) | 56.6 (50.4 to 62.7) | | |
| NHBA (M13520) | 55.1 (49.0 to 61.2) | 53.0 (46.8 to 59.1) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percentage of participants with 4-fold increase in hSBA titers against each of the N. meningitidis serogroup Men A, Men C, Men W and Men Y relative to baseline in both MenB+MenACWY and MenACWY Groups after MenACWY vaccination

| End point title | Percentage of participants with 4-fold increase in hSBA titers against each of the N. meningitidis serogroup Men A, Men C, Men W and Men Y relative to baseline in both MenB+MenACWY and MenACWY Groups after MenACWY vaccination[46] |
|---|---|

End point description:

The immune response to MenACWY vaccine is evaluated by measuring percentage of participants with 4-fold increase for the four serogroups Men A, Men C, Men W and Men Y. The Four-fold increase defined as: - For a pre-vaccination titer <LOD, a post-vaccination titer of >= 4-fold the LOD or >= LLOQ, whichever is greater, - For a pre-vaccination titer >=LOD but <LLOQ, a post vaccination titer of at least 4-fold the LLOQ, - For a pre-vaccination titer >= LLOQ, a post vaccination titer of at least 4-fold the pre-vaccination titer. Analysis was performed on PPS population. Only those participants with data available at specified timepoint were included in analysis.

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

End point timeframe:

At 1 month after MenACWY vaccination (i.e at Day 31) relative to baseline (i.e. Day 1)

Notes:

[46] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: As specified in the Protocol, the analysis assesses the immune response to MenACWY in healthy subjects 16-18 years of age against each of the serogroups A, C, W and Y, at one month after the (study) vaccination with MenACWY.

| End point values | MenB+MenACWY Group | MenACWY Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 293 | 296 | | |
| Units: Percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Men A | 98.5 (96.1 to 99.6) | 98.1 (95.6 to 99.4) | | |
| Men C | 95.2 (92.1 to 97.4) | 95.6 (92.6 to 97.6) | | |
| Men W | 98.6 (96.5 to 99.6) | 97.9 (95.6 to 99.2) | | |
| Men Y | 98.6 (96.5 to 99.6) | 98.3 (96.1 to 99.4) | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Solicited AEs: within 7 days post-vaccination. Unsolicited AEs: within 30 days post-vaccination. All-cause mortality,SAEs,MAAEs, AEs leading to withdrawal, and AESIs: monitored from Day 1 to study end at Day 271 or Day 451, depending on participation date

| | |
|---|---|
| Assessment type | Systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 27.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | MenB+MenACWY Group |

Reporting group description:

Participants received 1 dose of rMenB+OMV NZ vaccine administered concomitantly with 1 dose of MenACWY vaccine, as separate injections in each arm at Day 1, 1 dose of rMenB+OMV NZ vaccine at Day 61 and 1 dose of placebo at Day 91.

| | |
|---|---|
| Reporting group title | MenACWY Group |

Reporting group description:

Participants received 1 dose of MenACWY vaccine administered concomitantly with 1 dose of placebo, as separate injections in each arm at Day1, 1 dose of rMenB+OMV NZ vaccine each administered at Day 61 and at Day 91.

| | |
|---|---|
| Reporting group title | MenB Group |

Reporting group description:

Participants received 1 dose of rMenB+OMV NZ vaccine administered concomitantly with 1 dose of placebo, as separate injections in each arm at Day 1, 1 dose of rMenB+OMV NZ vaccine at Day 61 and 1 dose of MenACWY at Day 91.

| Serious adverse events | MenB+MenACWY Group | MenACWY Group | MenB Group |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 310 (0.65%) | 7 / 320 (2.19%) | 4 / 308 (1.30%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Injury, poisoning and procedural complications | | | |
| Fibula fracture | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Lumbar vertebral fracture | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pregnancy, puerperium and perinatal | | | |

| | | | |
|---|---|---|---|
| conditions | | | |
| Abortion spontaneous | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Adjustment disorder with depressed mood | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Depression | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Drug abuse | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Major depression | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Suicidal ideation | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 2 / 308 (0.65%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rhabdomyolysis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Appendicitis | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

Frequency threshold for reporting non-serious adverse events: 0 %

| **Non-serious adverse events** | MenB+MenACWY Group | MenACWY Group | MenB Group |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 293 / 310 (94.52%) | 289 / 320 (90.31%) | 293 / 308 (95.13%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Melanocytic naevus | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Vascular disorders | | | |
| Pallor | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Feeling of body temperature change | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Injection site pain | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 1 | 0 | 1 |
| Injection site hypoaesthesia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Injection site bruising | | | |
| subjects affected / exposed | 3 / 310 (0.97%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 3 | 0 | 2 |
| Induration | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Influenza like illness | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 2 / 308 (0.65%) |
| occurrences (all) | 1 | 0 | 2 |
| Fatigue | | | |
| subjects affected / exposed | 152 / 310 (49.03%) | 159 / 320 (49.69%) | 160 / 308 (51.95%) |
| occurrences (all) | 265 | 303 | 306 |
| Chills | | | |
| subjects affected / exposed | 2 / 310 (0.65%) | 3 / 320 (0.94%) | 2 / 308 (0.65%) |
| occurrences (all) | 2 | 3 | 3 |
| Chest pain | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 1 | 1 |
| Chest discomfort | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Administration site swelling | | | |
| subjects affected / exposed | 31 / 310 (10.00%) | 26 / 320 (8.13%) | 32 / 308 (10.39%) |
| occurrences (all) | 38 | 33 | 44 |
| Administration site pain | | | |
| subjects affected / exposed | 281 / 310 (90.65%) | 268 / 320 (83.75%) | 282 / 308 (91.56%) |
| occurrences (all) | 589 | 629 | 597 |
| Administration site induration | | | |
| subjects affected / exposed | 31 / 310 (10.00%) | 25 / 320 (7.81%) | 35 / 308 (11.36%) |
| occurrences (all) | 46 | 33 | 56 |
| Administration site erythema | | | |
| subjects affected / exposed | 28 / 310 (9.03%) | 28 / 320 (8.75%) | 31 / 308 (10.06%) |
| occurrences (all) | 39 | 30 | 37 |
| Vaccination site erythema | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Vaccination site bruising | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Vaccination site swelling | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Injection site pruritus | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Injection site reaction | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Injection site swelling | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Malaise | | | |
| subjects affected / exposed | 2 / 310 (0.65%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Pain | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 1 | 0 | 1 |
| Peripheral swelling | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 14 / 310 (4.52%) | 19 / 320 (5.94%) | 23 / 308 (7.47%) |
| occurrences (all) | 17 | 21 | 26 |
| Swelling | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 1 | 1 |
| Vaccination site rash | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Immune system disorders | | | |

| | | | |
|---|---|---|---|
| Multiple allergies | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Reproductive system and breast disorders | | | |
| Dysmenorrhoea | | | |
| subjects affected / exposed | 5 / 310 (1.61%) | 5 / 320 (1.56%) | 2 / 308 (0.65%) |
| occurrences (all) | 7 | 5 | 2 |
| Abnormal uterine bleeding | | | |
| subjects affected / exposed | 2 / 310 (0.65%) | 0 / 320 (0.00%) | 2 / 308 (0.65%) |
| occurrences (all) | 2 | 0 | 2 |
| Gynaecomastia | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Pelvic pain | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Vaginal discharge | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Varicocele | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Heavy menstrual bleeding | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Rhinorrhoea | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 3 / 320 (0.94%) | 1 / 308 (0.32%) |
| occurrences (all) | 1 | 3 | 1 |
| Asthma | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 1 / 320 (0.31%) | 1 / 308 (0.32%) |
| occurrences (all) | 1 | 1 | 1 |
| Cough | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 8 / 320 (2.50%) | 3 / 308 (0.97%) |
| occurrences (all) | 1 | 8 | 3 |
| Dysphonia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 1 / 320 (0.31%) | 1 / 308 (0.32%) |
| occurrences (all) | 1 | 1 | 1 |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nasal congestion | | | |
| subjects affected / exposed | 7 / 310 (2.26%) | 5 / 320 (1.56%) | 3 / 308 (0.97%) |
| occurrences (all) | 7 | 5 | 3 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 13 / 310 (4.19%) | 10 / 320 (3.13%) | 11 / 308 (3.57%) |
| occurrences (all) | 13 | 10 | 11 |
| Respiratory disorder | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Respiratory symptom | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Rhinitis allergic | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Sinus congestion | | | |
| subjects affected / exposed | 2 / 310 (0.65%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 2 | 0 | 1 |
| Sneezing | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Throat irritation | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Upper respiratory tract congestion | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Wheezing | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Depression | | | |
| subjects affected / exposed | 2 / 310 (0.65%) | 1 / 320 (0.31%) | 2 / 308 (0.65%) |
| occurrences (all) | 2 | 1 | 2 |
| Generalised anxiety disorder | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Intentional self-injury | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Investigations | | | |
| Arthroscopy | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Blood cholesterol increased | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Injury, poisoning and procedural complications | | | |
| Abdominal injury | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Breast procedural complication | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Concussion | | | |
| subjects affected / exposed | 2 / 310 (0.65%) | 0 / 320 (0.00%) | 3 / 308 (0.97%) |
| occurrences (all) | 2 | 0 | 3 |
| Contusion | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 3 / 320 (0.94%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 3 | 1 |
| Distal clavicular osteolysis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Eye injury | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Thermal burn | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Fibula fracture | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Foot fracture | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Head injury | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Joint injury | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Ligament injury | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Ligament rupture | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Ligament sprain | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 3 / 320 (0.94%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 3 | 1 |
| Limb injury | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 4 / 308 (1.30%) |
| occurrences (all) | 0 | 0 | 5 |
| Lip injury | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Muscle strain | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 310 (0.32%) | 1 / 320 (0.31%) | 1 / 308 (0.32%) |
| occurrences (all) | 1 | 1 | 1 |
| Open globe injury | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Procedural pain | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 1 / 320 (0.31%) | 2 / 308 (0.65%) |
| occurrences (all) | 1 | 1 | 2 |
| Scar | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Seroma | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin laceration | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 1 | 0 | 1 |
| Suture related complication | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Face injury | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Torus fracture | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vulvovaginal injury | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Congenital, familial and genetic disorders | | | |
| Os trigonum | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cardiac disorders | | | |

| | | | |
|---|---|---|---|
| Tachycardia | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 2 / 320 (0.63%) | 3 / 308 (0.97%) |
| occurrences (all) | 1 | 2 | 3 |
| Headache | | | |
| subjects affected / exposed | 178 / 310 (57.42%) | 185 / 320 (57.81%) | 185 / 308 (60.06%) |
| occurrences (all) | 320 | 345 | 317 |
| Migraine | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 1 | 0 | 1 |
| Paraesthesia | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sciatica | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sinus headache | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Blood and lymphatic system disorders | | | |
| Neutropenia | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Lymphadenopathy | | | |
| subjects affected / exposed | 2 / 310 (0.65%) | 2 / 320 (0.63%) | 0 / 308 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Ear and labyrinth disorders | | | |
| Eustachian tube dysfunction | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Ear pain | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 3 / 320 (0.94%) | 0 / 308 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Cerumen impaction | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 1 | 1 |
| Tympanic membrane perforation | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Eye disorders | | | |
| Astigmatism | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Episcleritis | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Lacrimation increased | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Myopia | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Blepharitis | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Photophobia | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Ocular hyperaemia | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gastrointestinal disorders | | | |
| Constipation | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Colitis | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Cheilitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Aphthous ulcer | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 5 / 320 (1.56%) | 4 / 308 (1.30%) |
| occurrences (all) | 0 | 5 | 5 |
| Abdominal pain | | | |
| subjects affected / exposed | 2 / 310 (0.65%) | 1 / 320 (0.31%) | 1 / 308 (0.32%) |
| occurrences (all) | 2 | 1 | 1 |
| Abdominal discomfort | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 2 / 308 (0.65%) |
| occurrences (all) | 1 | 0 | 2 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 4 / 320 (1.25%) | 2 / 308 (0.65%) |
| occurrences (all) | 1 | 6 | 2 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 4 / 310 (1.29%) | 6 / 320 (1.88%) | 3 / 308 (0.97%) |
| occurrences (all) | 4 | 6 | 3 |
| Toothache | | | |
| subjects affected / exposed | 5 / 310 (1.61%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences (all) | 5 | 1 | 0 |
| Tooth impacted | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 2 / 320 (0.63%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Salivary gland mucocoele | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Nausea | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 74 / 310 (23.87%) | 94 / 320 (29.38%) | 90 / 308 (29.22%) |
| occurrences (all) | 105 | 132 | 119 |
| Skin and subcutaneous tissue disorders | | | |
| Acne | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 2 / 320 (0.63%) | 1 / 308 (0.32%) |
| occurrences (all) | 1 | 2 | 1 |
| Pruritus | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 2 / 308 (0.65%) |
| occurrences (all) | 0 | 1 | 2 |
| Cold sweat | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dermatitis atopic | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Dermatitis contact | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Hirsutism | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pityriasis rosea | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Alopecia | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rash | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 4 / 308 (1.30%) |
| occurrences (all) | 0 | 0 | 4 |
| Rash pruritic | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Urticaria | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 1 | 0 | 1 |

| | | | |
|---|---|---|---|
| Sensitive skin | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Renal and urinary disorders | | | |
| Dysuria | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 3 / 320 (0.94%) | 0 / 308 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Micturition urgency | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Endocrine disorders | | | |
| Polycystic ovarian syndrome | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 1 | 1 |
| Musculoskeletal and connective tissue disorders | | | |
| Rotator cuff syndrome | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Arthralgia | | | |
| subjects affected / exposed | 53 / 310 (17.10%) | 58 / 320 (18.13%) | 46 / 308 (14.94%) |
| occurrences (all) | 65 | 77 | 66 |
| Back pain | | | |
| subjects affected / exposed | 2 / 310 (0.65%) | 2 / 320 (0.63%) | 0 / 308 (0.00%) |
| occurrences (all) | 2 | 2 | 0 |
| Bone swelling | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Joint range of motion decreased | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Joint swelling | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 1 | 1 |
| Medial tibial stress syndrome | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |

| | | | |
|---|---|---|---|
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Myalgia | | | |
| subjects affected / exposed | 73 / 310 (23.55%) | 88 / 320 (27.50%) | 81 / 308 (26.30%) |
| occurrences (all) | 86 | 116 | 112 |
| Neck pain | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 1 | 0 | 1 |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 2 / 320 (0.63%) | 3 / 308 (0.97%) |
| occurrences (all) | 1 | 2 | 3 |
| Pain in jaw | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Synovial cyst | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tendonitis | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 1 | 1 |
| Tendon pain | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Infections and infestations | | | |
| Acute sinusitis | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 3 / 320 (0.94%) | 3 / 308 (0.97%) |
| occurrences (all) | 0 | 3 | 3 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Beta haemolytic streptococcal infection | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Bacterial vulvovaginitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Bacterial vaginosis | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Bronchitis viral | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| COVID-19 | | | |
| subjects affected / exposed | 9 / 310 (2.90%) | 9 / 320 (2.81%) | 5 / 308 (1.62%) |
| occurrences (all) | 9 | 9 | 5 |
| Pharyngitis streptococcal | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 2 / 320 (0.63%) | 3 / 308 (0.97%) |
| occurrences (all) | 1 | 2 | 3 |
| Conjunctivitis | | | |
| subjects affected / exposed | 3 / 310 (0.97%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Conjunctivitis bacterial | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Eye infection | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Fungal infection | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 2 / 308 (0.65%) |
| occurrences (all) | 0 | 0 | 2 |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 1 / 320 (0.31%) | 2 / 308 (0.65%) |
| occurrences (all) | 1 | 1 | 2 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Gonorrhoea | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hordeolum | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Impetigo | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Influenza | | | |
| subjects affected / exposed | 4 / 310 (1.29%) | 2 / 320 (0.63%) | 10 / 308 (3.25%) |
| occurrences (all) | 4 | 2 | 10 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 11 / 310 (3.55%) | 18 / 320 (5.63%) | 4 / 308 (1.30%) |
| occurrences (all) | 11 | 18 | 5 |
| Otitis externa | | | |
| subjects affected / exposed | 2 / 310 (0.65%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Otitis media acute | | | |
| subjects affected / exposed | 3 / 310 (0.97%) | 1 / 320 (0.31%) | 2 / 308 (0.65%) |
| occurrences (all) | 3 | 1 | 3 |
| Pharyngitis | | | |
| subjects affected / exposed | 2 / 310 (0.65%) | 4 / 320 (1.25%) | 3 / 308 (0.97%) |
| occurrences (all) | 2 | 4 | 3 |
| Chlamydial infection | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 1 | 0 | 1 |
| Pharyngotonsillitis | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Pilonidal disease | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pyuria | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Respiratory tract infection viral | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 1 / 320 (0.31%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Rhinitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 310 (0.32%) | 1 / 320 (0.31%) | 2 / 308 (0.65%) |
| occurrences (all) | 1 | 1 | 3 |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 2 / 308 (0.65%) |
| occurrences (all) | 1 | 0 | 2 |
| Sinusitis bacterial | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Staphylococcal infection | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Stitch abscess | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 4 / 310 (1.29%) | 10 / 320 (3.13%) | 1 / 308 (0.32%) |
| occurrences (all) | 5 | 10 | 1 |
| Urethritis | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 2 / 320 (0.63%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 2 | 1 |
| Viral infection | | | |
| subjects affected / exposed | 3 / 310 (0.97%) | 0 / 320 (0.00%) | 3 / 308 (0.97%) |
| occurrences (all) | 3 | 0 | 3 |
| Viral pharyngitis | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 0 / 320 (0.00%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 0 | 1 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 1 / 320 (0.31%) | 2 / 308 (0.65%) |
| occurrences (all) | 1 | 1 | 2 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 310 (0.00%) | 1 / 320 (0.31%) | 1 / 308 (0.32%) |
| occurrences (all) | 0 | 1 | 1 |

| | | | |
|---|---|---|---|
| Dehydration | | | |
| subjects affected / exposed | 1 / 310 (0.32%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 2 / 310 (0.65%) | 0 / 320 (0.00%) | 0 / 308 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 14 August 2019 | As per the recommendation from CBER the study has been amended to include an update in development and validation of a new "agar-overlay" serum bactericidal assay using human serum complement (hSBA). Additional changes include validation of the MenB manual to measure immunogenicity of the meningococcal group B vaccine, a modification in the definition of 4-fold increase in post-vaccination hSBA titer definition when the pre-vaccination titer is below the limit of detection, and a modification in the population set to be used for safety analysis wherein the exposed set is to be used for all safety analyses. |
| 23 January 2020 | The inclusion of a booster recommendation in Menveo's US Prescription Insert, with the recommendation to administer the booster at least 4 years after the priming dose, has only been approved by US FDA in December 2019. As a result, the company intends to align the inclusion criterion in the V72_79 study with the recently introduced booster recommendation in the US and amend the protocol accordingly to allow inclusion of subjects who have received a meningococcal ACWY vaccine 4 years or greater in the past. |
| 21 June 2022 | The purpose of the amendment is to update the exclusion criteria of the protocol, align COVID-19 reporting requirements to local guidelines, and to update the definition of End of Study (EoS). |
| 11 October 2022 | The purpose of the amendment is to shorten the safety follow-up period to 6 months in<br>subjects who have not reached the 6-month safety follow-up after the last dose and to extend the visit window to 28 days post reference day to mitigate the impact of COVID pandemic, including quarantine, mandatory vaccination, or other disturbances in the study procedures. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported