

**Clinical trial results:****A Phase 2, Open-Label, Single-Center, Extension Study Evaluating Antibody Persistence compared to Naïve Children and Safety, Tolerability and Immunogenicity of Booster Doses of Novartis rMenB±OMV NZ Vaccine in Healthy UK Children Who Previously Received One or Four Doses of the Novartis Vaccine as Infants in Study V72P6.**

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

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2009-013054-33 |
| Trial protocol | GB |
| Global end of trial date | 22 May 2012 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v2 (current) |
| This version publication date | 10 June 2016 |
| First version publication date | 01 November 2014 |
| Version creation reason | |

Trial information**Trial identification**

| | |
|-----------------------|---------|
| Sponsor protocol code | V72P6E1 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01027351 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Novartis Vaccines and Diagnostics SRL |
| Sponsor organisation address | Via Fiorentina 1, Siena, Italy, 53100 |
| Public contact | Novartis Vaccines and Diagnostics SRL, Novartis Vaccines and Diagnostics SRL, RegistryContactVaccinesUS@novartis.com |
| Scientific contact | Novartis Vaccines and Diagnostics SRL, Novartis Vaccines and Diagnostics SRL, RegistryContactVaccinesUS@novartis.com |

Notes:

Paediatric regulatory details

| | |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMA-000139-PIP01-07 |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No | Yes |

Notes:

Results analysis stage

| | |
|--|--------------|
| Analysis stage | Final |
| Date of interim/final analysis | 10 June 2013 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|-------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 22 May 2012 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The present study, V72P6E1, is an extension of V72P6. The primary objective of this extension study will be to explore antibody persistence at approximately 40 months of age in subjects who received rMenB or rMenB+OMV NZ at 2, 4, 6 and 12 months of age in parent study V72P6.

Protection of trial subjects:

Study vaccines were not administered to individuals with known hypersensitivity to any component of the vaccines.

An oral temperature $\geq 38.0^{\circ}\text{C}$ ($\geq 100.4^{\circ}\text{F}$) or serious active infection was a reason for delaying vaccination.

Standard immunization practices were observed and care was taken to administer the injection intramuscularly. As with all injectable vaccines, appropriate medical treatment and supervision was readily available in case of rare anaphylactic reactions following administration of the study vaccine. Epinephrine 1:1000 and diphenhydramine was available in case of any anaphylactic reactions. Care was taken to ensure that the vaccine is not injected into a blood vessel.

Background therapy: -

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 12 January 2010 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects**Subjects enrolled per country**

| | |
|--------------------------------------|---------------------|
| Country: Number of subjects enrolled | United Kingdom: 163 |
| Worldwide total number of subjects | 163 |
| EEA total number of subjects | 163 |

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) | 163 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited from one centre in the United Kingdom.

Pre-assignment

Screening details:

All subjects were included in the trial.

Pre-assignment period milestones

| | |
|------------------------------|-----|
| Number of subjects started | 163 |
| Number of subjects completed | 163 |

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | overall trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|--------|
| Are arms mutually exclusive? | Yes |
| Arm title | 5rMenB |

Arm description:

Subjects who had received four doses of rMenB vaccine (at 2,4,6 and 12 months of age) in the parent study were administered a fifth dose of rMenB vaccine, at 40 months of age in the present study.

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Meningococcal (group B) multicomponent recombinant adsorbed vaccine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection in pre-filled syringe |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects were administered 1 dose of 0.5 millilitres.

| | |
|------------------|---------------|
| Arm title | 5rMenB+OMV NZ |
|------------------|---------------|

Arm description:

Subjects who had received four doses of rMenB +OMV NZ vaccine (at 2,4,6 and 12 months of age) in the parent study were administered a fifth dose of rMenB +OMV NZ vaccine, at 40 months of age in the present study.

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Meningococcal (group B) multicomponent recombinant adsorbed vaccine plus Outer Membrane Vesicles New Zealand (OMV NZ) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection in pre-filled syringe |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects were administered 1 dose of 0.5 millilitres.

| | |
|------------------|--------|
| Arm title | 3rMenB |
|------------------|--------|

Arm description:

Subjects who had previously received one dose of rMenB vaccine (at 12 months of age) were administered two doses of rMenB vaccine, at 40 and 42 months of age in the present study.

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Meningococcal (group B) multicomponent recombinant adsorbed vaccine |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection in pre-filled syringe |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects were administered 2 doses of 0.5 millilitres.

| | |
|------------------|---------------|
| Arm title | 3rMenB+OMV NZ |
|------------------|---------------|

Arm description:

Subjects who had previously received one dose of rMenB +OMV NZ vaccine (at 12 months of age) were administered two doses of rMenB +OMV NZ vaccine, at 40 and 42 months of age in the present study.

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Meningococcal (group B) multicomponent recombinant adsorbed vaccine plus Outer Membrane Vesicles New Zealand (OMV NZ) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection in pre-filled syringe |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects were administered 2 doses of 0.5 millilitres.

| | |
|------------------|------------|
| Arm title | Naive_4042 |
|------------------|------------|

Arm description:

Vaccine-naïve subjects who received two catch-up doses of rMenB+OMV NZ vaccine at 40 and 42 months of age in the present study.

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Meningococcal (group B) multicomponent recombinant adsorbed vaccine plus Outer Membrane Vesicles New Zealand (OMV NZ) |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection in pre-filled syringe |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects were administered 2 doses of 0.5 millilitres.

| | |
|------------------|------------|
| Arm title | Naive_6062 |
|------------------|------------|

Arm description:

Vaccine-naïve subjects who received two catch-up doses of rMenB+OMV NZ vaccine at 60 and 62 months of age in the present study.

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Meningococcal (group B) multicomponent recombinant adsorbed vaccine plus OMV NZ |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection in pre-filled syringe |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Subjects were administered 2 doses of 0.5 millilitres.

| Number of subjects in period 1 | 5rMenB | 5rMenB+OMV NZ | 3rMenB |
|---------------------------------------|--------|---------------|--------|
| Started | 29 | 19 | 14 |
| Completed | 26 | 18 | 13 |
| Not completed | 3 | 1 | 1 |
| Consent withdrawn by subject | 1 | - | 1 |
| Lost to follow-up | 1 | 1 | - |
| inappropriate enrollment | - | - | - |
| Protocol deviation | 1 | - | - |

| Number of subjects in period 1 | 3rMenB+OMV NZ | Naive_4042 | Naive_6062 |
|---------------------------------------|---------------|------------|------------|
| Started | 8 | 43 | 50 |
| Completed | 6 | 32 | 45 |
| Not completed | 2 | 11 | 5 |
| Consent withdrawn by subject | - | 3 | 5 |
| Lost to follow-up | 1 | 6 | - |
| inappropriate enrollment | - | 1 | - |
| Protocol deviation | 1 | 1 | - |

Baseline characteristics

Reporting groups

| | |
|--|---------------|
| Reporting group title | 5rMenB |
| Reporting group description: Subjects who had received four doses of rMenB vaccine (at 2,4,6 and 12 months of age) in the parent study were administered a fifth dose of rMenB vaccine, at 40 months of age in the present study. | |
| Reporting group title | 5rMenB+OMV NZ |
| Reporting group description: Subjects who had received four doses of rMenB +OMV NZ vaccine (at 2,4,6 and 12 months of age) in the parent study were administered a fifth dose of rMenB +OMV NZ vaccine, at 40 months of age in the present study. | |
| Reporting group title | 3rMenB |
| Reporting group description: Subjects who had previously received one dose of rMenB vaccine (at 12 months of age) were administered two doses of rMenB vaccine, at 40 and 42 months of age in the present study. | |
| Reporting group title | 3rMenB+OMV NZ |
| Reporting group description: Subjects who had previously received one dose of rMenB +OMV NZ vaccine (at 12 months of age) were administered two doses of rMenB +OMV NZ vaccine, at 40 and 42 months of age in the present study. | |
| Reporting group title | Naive_4042 |
| Reporting group description: Vaccine-naïve subjects who received two catch-up doses of rMenB+OMV NZ vaccine at 40 and 42 months of age in the present study. | |
| Reporting group title | Naive_6062 |
| Reporting group description: Vaccine-naïve subjects who received two catch-up doses of rMenB+OMV NZ vaccine at 60 and 62 months of age in the present study. | |

| Reporting group values | 5rMenB | 5rMenB+OMV NZ | 3rMenB |
|------------------------------------|--------|---------------|--------|
| Number of subjects | 29 | 19 | 14 |
| Age categorical Units: Subjects | | | |

| | | | |
|--|---------------|---------------|---------------|
| Age continuous Units: months arithmetic mean standard deviation | 41.4 ± 1.5 | 41.8 ± 1.4 | 41.4 ± 1.5 |
| Gender categorical Units: Subjects Female Male | 17 12 | 9 10 | 5 9 |

| Reporting group values | 3rMenB+OMV NZ | Naive_4042 | Naive_6062 |
|------------------------------------|---------------|------------|------------|
| Number of subjects | 8 | 43 | 50 |
| Age categorical Units: Subjects | | | |

| | | | |
|--|---------------|---------------|---------------|
| Age continuous Units: months arithmetic mean standard deviation | 40.4 ± 0.7 | 41.8 ± 1.7 | 61.3 ± 0.9 |
| Gender categorical Units: Subjects | | | |
| Female | 3 | 23 | 27 |
| Male | 5 | 20 | 23 |

| | | | |
|------------------------------------|-------|--|--|
| Reporting group values | Total | | |
| Number of subjects | 163 | | |
| Age categorical Units: Subjects | | | |

| | | | |
|--|----|--|--|
| Age continuous Units: months arithmetic mean standard deviation | - | | |
| Gender categorical Units: Subjects | | | |
| Female | 84 | | |
| Male | 79 | | |

Subject analysis sets

| | |
|----------------------------|---|
| Subject analysis set title | MITT – 40 months of age antibody persistence population |
| Subject analysis set type | Modified intention-to-treat |

Subject analysis set description:

MITT – 40 months of age antibody persistence population (groups 5rMenB, 5rMenB+OMV, 3rMenB, 3rMenB+OMV, Naive_4042). All subjects in the all enrolled population who: provided an evaluable serum sample at 40 months of age, (ie at visit 1 of V72P6E1 for groups 5rMenB, 5rMenB+OMV, 3rMenB, 3rMenB+OMV and Naive_4042).

| | |
|----------------------------|---|
| Subject analysis set title | MITT – 60 Months of Age Antibody Persistence population |
| Subject analysis set type | Modified intention-to-treat |

Subject analysis set description:

MITT – 60 Months of Age Antibody Persistence population (5rMenB, 5rMenB+OMV NZ, 3rMenB, 3rMenB+OMV NZ, Naive_4042, Naive_6062). All subjects in the All Enrolled Set who provide an evaluable serum sample at 60 Months of Age (Visit 3 of V72P6E1 for groups 5rMenB and 5rMenB+OMV NZ, Visit 5 for Groups 3rMenB, 3rMenB+OMV NZ, Naive_4042, Visit 1 for Group Naive_6062).

| | |
|----------------------------|------------------------------------|
| Subject analysis set title | MITT – Booster Response population |
| Subject analysis set type | Modified intention-to-treat |

Subject analysis set description:

MITT – Booster Response population (Groups 5rMenB, 5rMenB+OMV, 3rMenB, 3rMenB+OMV, Naive_4042, Naive_6062). For Groups 5rMenB, 5rMenB+OMV, 3rMenB, 3rMenB+OMV, Naive_4042, all subjects in the All enrolled set who:

- receive a study vaccination in the present V72P6E1 study; and
- provide an evaluable serum sample either, at one month after the (first) (booster) dose (Visit 2) or at one month after the second (booster) dose (for Groups 3rMenB, 3rMenB+OMV, Naive_4042 Visit 4);

For Group Naive_6062, all subjects in the All enrolled set who provide an evaluable serum sample at 60 Months of Age (Visit 1).

| | |
|----------------------------|-----------------|
| Subject analysis set title | Exposed set |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

All enrolled subjects who actually receive a rMenB + OMV vaccination

| | |
|----------------------------|-----------------|
| Subject analysis set title | Safety Set |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

All subjects in the exposed set who provided post-baseline safety data

| | |
|----------------------------|--|
| Subject analysis set title | MITT – Two Dose Catch Up Schedule population |
| Subject analysis set type | Modified intention-to-treat |

Subject analysis set description:

MITT – Two Dose Catch Up Schedule population (Groups Naive_4042 and Naive_6062). All subjects in the All enrolled set who:

- received a study vaccination in the present V72P6E1 study; and
- provided an evaluable serum sample either, at one month after the first dose (Visit 2 for Naive_4042 only) or at one month after the second dose (Visit 4 for Group Naive_4042 and Visit 3 for Group Naive_6062).

| Reporting group values | MITT – 40 months of age antibody persistence population | MITT – 60 Months of Age Antibody Persistence population | MITT – Booster Response population |
|------------------------------------|---|---|------------------------------------|
| Number of subjects | 108 | 134 | 160 |
| Age categorical Units: Subjects | | | |

| | | | |
|--|---------------|---------------|---------------|
| Age continuous Units: months arithmetic mean standard deviation | 41.5 ± 1.6 | 48.4 ± 9.6 | 47.7 ± 9.3 |
| Gender categorical Units: Subjects | | | |
| Female | 54 | 68 | 83 |
| Male | 54 | 66 | 77 |

| Reporting group values | Exposed set | Safety Set | MITT – Two Dose Catch Up Schedule population |
|------------------------------------|-------------|------------|--|
| Number of subjects | 162 | 162 | 152 |
| Age categorical Units: Subjects | | | |

| | | | |
|--|---------------|---------------|-----------|
| Age continuous Units: months arithmetic mean standard deviation | 47.6 ± 9.3 | 47.6 ± 9.3 | 47 ± 9 |
| Gender categorical Units: Subjects | | | |
| Female | 84 | 84 | 80 |
| Male | 78 | 78 | 72 |

End points

End points reporting groups

| | |
|--|---|
| Reporting group title | 5rMenB |
| Reporting group description: Subjects who had received four doses of rMenB vaccine (at 2,4,6 and 12 months of age) in the parent study were administered a fifth dose of rMenB vaccine, at 40 months of age in the present study. | |
| Reporting group title | 5rMenB+OMV NZ |
| Reporting group description: Subjects who had received four doses of rMenB +OMV NZ vaccine (at 2,4,6 and 12 months of age) in the parent study were administered a fifth dose of rMenB +OMV NZ vaccine, at 40 months of age in the present study. | |
| Reporting group title | 3rMenB |
| Reporting group description: Subjects who had previously received one dose of rMenB vaccine (at 12 months of age) were administered two doses of rMenB vaccine, at 40 and 42 months of age in the present study. | |
| Reporting group title | 3rMenB+OMV NZ |
| Reporting group description: Subjects who had previously received one dose of rMenB +OMV NZ vaccine (at 12 months of age) were administered two doses of rMenB +OMV NZ vaccine, at 40 and 42 months of age in the present study. | |
| Reporting group title | Naive_4042 |
| Reporting group description: Vaccine-naïve subjects who received two catch-up doses of rMenB+OMV NZ vaccine at 40 and 42 months of age in the present study. | |
| Reporting group title | Naive_6062 |
| Reporting group description: Vaccine-naïve subjects who received two catch-up doses of rMenB+OMV NZ vaccine at 60 and 62 months of age in the present study. | |
| Subject analysis set title | MITT – 40 months of age antibody persistence population |
| Subject analysis set type | Modified intention-to-treat |
| Subject analysis set description: MITT – 40 months of age antibody persistence population (groups 5rMenB, 5rMenB+OMV, 3rMenB, 3rMenB+OMV, Naive_4042). All subjects in the all enrolled population who: provided an evaluable serum sample at 40 months of age, (ie at visit 1 of V72P6E1 for groups 5rMenB, 5rMenB+OMV, 3rMenB, 3rMenB+OMV and Naive_4042). | |
| Subject analysis set title | MITT – 60 Months of Age Antibody Persistence population |
| Subject analysis set type | Modified intention-to-treat |
| Subject analysis set description: MITT – 60 Months of Age Antibody Persistence population (5rMenB, 5rMenB+OMV NZ, 3rMenB, 3rMenB+OMV NZ, Naive_4042, Naive_6062). All subjects in the All Enrolled Set who provide an evaluable serum sample at 60 Months of Age (Visit 3 of V72P6E1 for groups 5rMenB and 5rMenB+OMV NZ, Visit 5 for Groups 3rMenB, 3rMenB+OMV NZ, Naive_4042, Visit 1 for Group Naive_6062). | |
| Subject analysis set title | MITT – Booster Response population |
| Subject analysis set type | Modified intention-to-treat |
| Subject analysis set description: MITT – Booster Response population (Groups 5rMenB, 5rMenB+OMV, 3rMenB, 3rMenB+OMV, Naive_4042, Naive_6062). For Groups 5rMenB, 5rMenB+OMV, 3rMenB, 3rMenB+OMV, Naive_4042, all subjects in the All enrolled set who: <ul style="list-style-type: none">▫ receive a study vaccination in the present V72P6E1 study; and▫ provide an evaluable serum sample either, at one month after the (first) (booster) dose (Visit 2) or at one month after the second (booster) dose (for Groups 3rMenB, 3rMenB+OMV, Naive_4042 Visit 4); For Group Naive_6062, all subjects in the All enrolled set who provide an evaluable serum sample at 60 Months of Age (Visit 1). | |
| Subject analysis set title | Exposed set |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

All enrolled subjects who actually receive a rMenB + OMV vaccination

| | |
|----------------------------|-----------------|
| Subject analysis set title | Safety Set |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

All subjects in the exposed set who provided post-baseline safety data

| | |
|----------------------------|--|
| Subject analysis set title | MITT – Two Dose Catch Up Schedule population |
| Subject analysis set type | Modified intention-to-treat |

Subject analysis set description:

MITT – Two Dose Catch Up Schedule population (Groups Naive_4042 and Naive_6062). All subjects in the All enrolled set who:

- received a study vaccination in the present V72P6E1 study; and
- provided an evaluable serum sample either, at one month after the first dose (Visit 2 for Naive_4042 only) or at one month after the second dose (Visit 4 for Group Naive_4042 and Visit 3 for Group Naive_6062).

Primary: 1) Persistence of geometric mean antibody titers in children (who previously received 4 doses of Men B vaccine), at 40 months of age

| | |
|-----------------|--|
| End point title | 1) Persistence of geometric mean antibody titers in children (who previously received 4 doses of Men B vaccine), at 40 months of age ^{[1][2]} |
|-----------------|--|

End point description:

Persistence of geometric mean titers (GMTs) against N.meningitidis B strains in children (at 40 months of age) who had previously received four doses of either rMenB or rMen+OMV NZ vaccines in parent study, are compared with the GMTs in vaccine-naïve children.

Analysis was done on the MITT – 40 months of age antibody persistence population.

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

End point timeframe:

28 months after last vaccination; Baseline for Naïve

Notes:

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

Justification: There was no statistical null hypothesis associated with this immunogenicity objective.

[2] - 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: There was no statistical null hypothesis associated with this immunogenicity objective.

| End point values | 5rMenB | 5rMenB+OMV NZ | Naive_4042 | |
|--|---------------------|---------------------|--------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 29 | 17 | 40 | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| H 44/76 strain | 3.24 (2.33 to 4.52) | 5.34 (3.47 to 8.23) | 4.25 (3.22 to 5.6) | |
| 5/99 strain (N=28, 17, 40) | 5.11 (2.33 to 11) | 28 (10 to 77) | 1.11 (0.9 to 1.36) | |
| NZ 98/254 strain | 1.09 (0.79 to 1.51) | 2.77 (1.81 to 4.23) | 1 (1 to 1) | |
| M10713 strain (N=28, 15, 40) | 9.15 (5.01 to 17) | 5.34 (2.35 to 12) | 8.75 (5.22 to 15) | |

Statistical analyses

No statistical analyses for this end point

Primary: 2) Percentage of subjects (who previously received 4 doses of Men B vaccine) with persisting serum bactericidal antibody titers $\geq 1:4$ and $\geq 1:8$ at 40 months of age

| | |
|-----------------|---|
| End point title | 2) Percentage of subjects (who previously received 4 doses of Men B vaccine) with persisting serum bactericidal antibody titers $\geq 1:4$ and $\geq 1:8$ at 40 months of age ^{[3][4]} |
|-----------------|---|

End point description:

The percentages of subjects with persisting serum bactericidal antibodies (hSBA) titers $\geq 1:4$ and $\geq 1:8$, against N.meningitidis B strains at 40 months of age who had previously received four doses of either rMenB or rMen+OMV NZ vaccines in parent study are reported.

The serum bactericidal antibodies directed against serogroup B meningococci, are measured by human complement Serum Bactericidal Assay (hSBA).

Analysis was done on the MITT – 40 months of age antibody persistence population.

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

End point timeframe:

28 months after last vaccination; Baseline for Naïve

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: There was no statistical null hypothesis associated with this immunogenicity objective.

[4] - 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: There was no statistical null hypothesis associated with this immunogenicity objective.

| End point values | 5rMenB | 5rMenB+OMV NZ | Naive_4042 | |
|------------------------------------|-----------------|-----------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 29 | 17 | 40 | |
| Units: percentages of subjects | | | | |
| number (confidence interval 95%) | | | | |
| hSBA $\geq 1:4$ (H44/76 strain) | 45 (26 to 64) | 65 (38 to 86) | 63 (46 to 77) | |
| hSBA $\geq 1:4$ (5/99 strain) | 43 (24 to 63) | 76 (50 to 93) | 3 (0.063 to 13) | |
| hSBA $\geq 1:4$ (NZ 98/254 strain) | 3 (0.087 to 18) | 41 (18 to 67) | 0 (0 to 9) | |
| hSBA $\geq 1:4$ (M10713 strain) | 68 (48 to 84) | 67 (38 to 88) | 68 (51 to 81) | |
| hSBA $\geq 1:8$ (H44/76 strain) | 14 (4 to 32) | 35 (14 to 62) | 30 (17 to 47) | |
| hSBA $\geq 1:8$ (5/99 strain) | 43 (24 to 63) | 76 (50 to 93) | 3 (0.063 to 13) | |
| hSBA $\geq 1:8$ (NZ 98/254 strain) | 0 (0 to 12) | 24 (7 to 50) | 0 (0 to 9) | |
| hSBA $\geq 1:8$ (M10713 strain) | 61 (41 to 78) | 40 (16 to 68) | 45 (29 to 62) | |

Statistical analyses

No statistical analyses for this end point

Primary: 3) Number of subjects reporting solicited adverse events after receiving one or two booster doses of rMen B or rMenB+OMV NZ vaccine at 40 months of age.

| | |
|-----------------|--|
| End point title | 3) Number of subjects reporting solicited adverse events after receiving one or two booster doses of rMen B or rMenB+OMV NZ vaccine at 40 months of age. ^{[5][6]} |
|-----------------|--|

End point description:

The safety and tolerability of one or two booster doses of rMen B or rMenB+OMV NZ vaccine administered at 40 months of age in children who had previously received one or four doses of the same vaccine as infants in parent study is assessed in terms of number of subjects with solicited local and systemic reactions following vaccination.

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

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

End point timeframe:

Day 1-7 after booster vaccination

Notes:

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

Justification: There was no statistical null hypothesis associated with this safety objective.

[6] - 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: There was no statistical null hypothesis associated with this safety objective.

| End point values | 5rMenB | 5rMenB+OMV NZ | 3rMenB | 3rMenB+OMV NZ |
|--|-----------------|------------------|-----------------|------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 29 | 19 | 14 | 8 |
| Units: Number of participants | | | | |
| Local | 28 | 19 | 14 | 8 |
| Injection-site pain | 17 | 14 | 8 | 8 |
| Injection-site erythema | 28 | 19 | 14 | 8 |
| Injection-site swelling | 13 | 5 | 9 | 4 |
| Injection-site induration | 14 | 9 | 8 | 6 |
| Systemic | 19 | 13 | 11 | 8 |
| Changes in eating habits | 5 | 10 | 5 | 4 |
| Sleepiness | 13 | 12 | 8 | 6 |
| Vomiting | 1 | 3 | 3 | 0 |
| Diarrhea | 3 | 1 | 3 | 1 |
| Irritability | 14 | 10 | 9 | 8 |
| Headache | 1 | 0 | 2 | 1 |
| Arthralgia | 0 | 6 | 4 | 4 |
| Rash | 3 | 0 | 2 | 1 |
| Fever ($\geq 38^{\circ}\text{C}$) | 1 | 1 | 4 | 0 |
| Other | 10 | 12 | 5 | 7 |
| Antipyretic preventive medication used | 10 | 12 | 3 | 7 |
| Antipyretic treatment medication used | 1 | 2 | 4 | 0 |
| Medically attended fever | 0 | 0 | 1 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: 4) Persistence of geometric mean antibody titers in children (who previously received one dose of Men B vaccine), at 40 months of age

| | |
|-----------------|--|
| End point title | 4) Persistence of geometric mean antibody titers in children (who previously received one dose of Men B vaccine), at 40 months of age ^[7] |
|-----------------|--|

End point description:

Persisting GMTs against N.meningitidis B strains in children (at 40 months of age) who had previously received one dose of either rMenB or rMen+OMV NZ vaccines in parent study, are compared with the GMTs in vaccine-naïve children.

Analysis was done on the MITT – 40 months of age antibody persistence population.

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

End point timeframe:

28 months after vaccination; baseline for Naïve

Notes:

[7] - 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: There was no statistical null hypothesis associated with this immunogenicity objective.

| End point values | 3rMenB | 3rMenB+OMV NZ | Naive_4042 | |
|---|------------------------|------------------------|-----------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 14 | 8 | 40 | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| H44/76 strain | 3.59 (1.8 to 7.15) | 3.47 (1.39 to 8.64) | 4.25 (3.22 to 5.6) | |
| 5/99 strain | 9.57 (3.88 to 24) | 1 (0.3 to 3.3) | 1.11 (0.9 to 1.36) | |
| NZ 98/254 strain | 1.23 (0.96 to 1.57) | 1 (0.72 to 1.38) | 1 (1 to 1) | |
| M10713 strain (N=13, 8, 40) | 3.26 (1.49 to 7.11) | 3 (1.11 to 8.11) | 8.75 (5.22 to 15) | |

Statistical analyses

No statistical analyses for this end point

Secondary: 5) Percentage of Subjects (Who Had Previously Received One Dose of Men B Vaccine) With Persisting Serum Bactericidal Antibody Titers $\geq 1:4$ and $\geq 1:8$ at 40 Months of Age

| | |
|-----------------|---|
| End point title | 5) Percentage of Subjects (Who Had Previously Received One Dose of Men B Vaccine) With Persisting Serum Bactericidal Antibody Titers $\geq 1:4$ and $\geq 1:8$ at 40 Months of Age ^[8] |
|-----------------|---|

End point description:

The percentages of subjects with persisting hSBA titers $\geq 1:4$ and $\geq 1:8$, against N.meningitidis B strains at 40 months of age who had previously received one dose of either rMenB or rMen+OMV NZ vaccines in parent study are reported.

Analysis was done on the MITT – 40 months of age antibody persistence population.

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

End point timeframe:

28 months after vaccination; baseline for naïve

Notes:

[8] - 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: There was no statistical null hypothesis associated with this immunogenicity objective.

| End point values | 3rMenB | 3rMenB+OMV NZ | Naive_4042 | |
|--|-----------------|------------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 14 | 8 | 40 | |
| Units: Percentages of subjects | | | | |
| number (confidence interval 95%) | | | | |
| hSBA \geq 1:4 (H44/76 strain) | 57 (29 to 82) | 38 (9 to 76) | 63 (46 to 77) | |
| hSBA \geq 1:4 (5/99 strain) | 57 (29 to 82) | 0 (0 to 37) | 3 (0.063 to 13) | |
| hSBA \geq 1:4 (NZ 98/254 strain) | 7 (0 to 34) | 0 (0 to 37) | 0 (0 to 9) | |
| hSBA \geq 1:4 (M10713 strain; N=13, 8, 40) | 54 (25 to 81) | 25 (3 to 65) | 68 (51 to 81) | |
| hSBA \geq 1:8 (H44/76 strain) | 7 (0 to 34) | 13 (0 to 53) | 30 (17 to 47) | |
| hSBA \geq 1:8 (5/99 strain) | 43 (18 to 71) | 0 (0 to 37) | 3 (0.063 to 13) | |
| hSBA \geq 1:8 (NZ 98/254 strain) | 0 (0 to 23) | 0 (0 to 37) | 0 (0 to 9) | |
| hSBA \geq 1:8 (M10713 strain; N=13, 8, 40) | 15 (2 to 45) | 13 (0 to 53) | 45 (29 to 62) | |

Statistical analyses

No statistical analyses for this end point

Secondary: 6) Geometric Mean Antibody Titers in Children (Who Previously Received 4 Doses of Men B Vaccine), After Receiving a Booster Dose of rMenB or rMenB+OMV NZ Vaccine at 40 Months of Age

| | |
|-----------------|--|
| End point title | 6) Geometric Mean Antibody Titers in Children (Who Previously Received 4 Doses of Men B Vaccine), After Receiving a Booster Dose of rMenB or rMenB+OMV NZ Vaccine at 40 Months of Age ^[9] |
|-----------------|--|

End point description:

The GMTs against N.meningitidis B strains in children (who had previously received four doses MenB vaccine in parent study) after a single booster dose of rMenB or rMenB+OMV NZ vaccine given at 40 months of age, are compared with the antibody titers following one catch-up dose rMenB+OMV NZ vaccine given at 40 months to vaccine-naïve subjects.

Analysis was done on the MITT – Booster Response population.

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

End point timeframe:

1 month post- booster/ dose 1 for Naïve

Notes:

[9] - 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: There was no statistical null hypothesis associated with this immunogenicity objective.

| End point values | 5rMenB | 5rMenB+OMV NZ | Naive_4042 | |
|--|---------------------|--------------------|-------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 29 | 19 | 38 | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| H44/76 strain | 99 (67 to 145) | 89 (56 to 141) | 12 (7.96 to 19) | |
| 5/99 strain (N=28, 18, 38) | 778 (448 to 1349) | 1708 (859 to 3396) | 22 (12 to 40) | |
| NZ 98/254 strain | 1.64 (0.95 to 2.85) | 47 (24 to 91) | 7.73 (4.62 to 13) | |

| | | | | |
|------------------------------|---------------|---------------|----------------|--|
| M10713 strain (N=28, 18, 38) | 38 (24 to 59) | 39 (22 to 67) | 11 (6.7 to 19) | |
|------------------------------|---------------|---------------|----------------|--|

Statistical analyses

No statistical analyses for this end point

Secondary: 7) Percentage of subjects (who previously received 4 doses of Men B vaccine) with serum bactericidal antibody titers $\geq 1:4$ and $\geq 1:8$ after receiving a booster dose of either rMenB or rMenB+OMV NZ vaccine at 40 months of age

| | |
|-----------------|---|
| End point title | 7) Percentage of subjects (who previously received 4 doses of Men B vaccine) with serum bactericidal antibody titers $\geq 1:4$ and $\geq 1:8$ after receiving a booster dose of either rMenB or rMenB+OMV NZ vaccine at 40 months of age ^[10] |
|-----------------|---|

End point description:

The percentages of subjects (who had previously received four doses MenB vaccine in parent study) with hSBA titers $\geq 1:4$ and $\geq 1:8$, against N.meningitidis B strains after receiving a single booster dose of either rMenB or rMen+OMV NZ vaccines at 40 months of age are compared with hSBA responses following one catch-up dose of rMenB+OMV NZ vaccine given at 40 months in vaccine-naïve subjects.

Analysis was done on the MITT – Booster Response population.

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

End point timeframe:

1 month post- booster/ dose 1 for Naïve

Notes:

[10] - 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: There was no statistical null hypothesis associated with this immunogenicity objective.

| End point values | 5rMenB | 5rMenB+OMV NZ | Naive_4042 | |
|------------------------------------|-----------------|-----------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 28 | 19 | 38 | |
| Units: Percentages of subjects | | | | |
| number (confidence interval 95%) | | | | |
| hSBA $\geq 1:4$ (H44/76 strain) | 100 (88 to 100) | 100 (82 to 100) | 89 (75 to 97) | |
| hSBA $\geq 1:4$ (5/99 strain) | 100 (88 to 100) | 100 (81 to 100) | 76 (60 to 89) | |
| hSBA $\geq 1:4$ (NZ 98/254 strain) | 14 (4 to 33) | 89 (67 to 99) | 66 (49 to 80) | |
| hSBA $\geq 1:4$ (M10713 strain) | 96 (82 to 100) | 94 (73 to 100) | 76 (60 to 89) | |
| hSBA $\geq 1:8$ (H44/76 strain) | 96 (82 to 100) | 100 (82 to 100) | 63 (46 to 78) | |
| hSBA $\geq 1:8$ (5/99 strain) | 100 (88 to 100) | 100 (81 to 100) | 71 (54 to 85) | |
| hSBA $\geq 1:8$ (NZ 98/254 strain) | 11 (2 to 28) | 89 (67 to 99) | 58 (41 to 74) | |
| hSBA $\geq 1:8$ (M10713 strain) | 89 (72 to 98) | 94 (73 to 100) | 61 (43 to 76) | |

Statistical analyses

Secondary: 8) Percentage of subjects (who previously received 4 doses of Men B vaccine) with 4-fold increase in serum bactericidal antibody titers after receiving a booster dose of either rMenB or rMenB+OMV NZ vaccine at 40 months of age

| | |
|-----------------|--|
| End point title | 8) Percentage of subjects (who previously received 4 doses of Men B vaccine) with 4-fold increase in serum bactericidal antibody titers after receiving a booster dose of either rMenB or rMenB+OMV NZ vaccine at 40 months of age ^[11] |
|-----------------|--|

End point description:

The percentages of subjects (who had previously received four doses MenB vaccine in parent study) showing a 4-fold increase in hSBA titers over baseline against N.meningitidis B strains, after receiving a booster dose of either rMenB or rMen+OMV NZ vaccines at 40 months of age are compared with hSBA responses following one catch-up dose of rMenB+OMV NZ vaccine given at 40 months in vaccine-naïve subjects.

Baseline is defined as either the time that the (first) booster dose was given or the time of the first vaccination in this study.

Analysis was done on the MITT – Booster Response population.

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

End point timeframe:

1 month post- booster/ dose 1 for Naïve

Notes:

[11] - 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: There was no statistical null hypothesis associated with this immunogenicity objective.

| End point values | 5rMenB | 5rMenB+OMV NZ | Naive_4042 | |
|----------------------------------|-----------------|-----------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 28 | 17 | 37 | |
| Units: Percentages of subjects | | | | |
| number (confidence interval 95%) | | | | |
| H44/76 strain | 89 (72 to 98) | 94 (71 to 100) | 41 (25 to 58) | |
| 5/99 strain (N=27, 16, 37) | 100 (87 to 100) | 94 (70 to 100) | 68 (50 to 82) | |
| NZ 98/254 strain | 11 (2 to 28) | 82 (57 to 96) | 57 (39 to 73) | |
| M10713 strain (N=27, 15, 37) | 41 (22 to 61) | 67 (38 to 88) | 14 (5 to 29) | |

Statistical analyses

No statistical analyses for this end point

Secondary: 9) Geometric mean antibody titers in children after receiving two booster doses of either rMenB or rMenB+OMV NZ vaccine at 40 & 42 months of age

| | |
|-----------------|--|
| End point title | 9) Geometric mean antibody titers in children after receiving two booster doses of either rMenB or rMenB+OMV NZ vaccine at 40 & 42 months of age ^[12] |
|-----------------|--|

End point description:

The GMTs against N.meningitidis B strains in children (who had previously received one dose MenB vaccine in parent study) after a two booster doses of either rMenB or rMenB+OMV NZ vaccine given at 40 & 42 months of age.

Analysis was done on the MITT – Booster Response population.

| | |
|--------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| 1 month post vaccination | |

Notes:

[12] - 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: There was no statistical null hypothesis associated with this immunogenicity objective.

| End point values | 3rMenB | 3rMenB+OMV NZ | Naive_4042 | |
|--|---------------------|---------------------|--------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 13 | 8 | 38 | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| H44/76 strain (dose 1; N=13, 7, 38) | 94 (48 to 185) | 76 (30 to 190) | 12 (7.96 to 19) | |
| H44/76 strain (dose 2; N=13, 8, 36) | 127 (81 to 198) | 145 (82 to 255) | 88 (66 to 117) | |
| 5/99 strain (dose 1; N=13, 7, 38) | 2379 (1164 to 4859) | 509 (192 to 1348) | 22 (12 to 40) | |
| 5/99 strain (dose 2; N=13, 8, 36) | 5240 (3082 to 8911) | 2413 (1226 to 4747) | 1019 (762 to 1362) | |
| NZ 98/254 strain (dose 1; N=13, 7, 38) | 1.73 (0.86 to 3.48) | 148 (57 to 384) | 7.73 (4.62 to 13) | |
| NZ 98/254 strain (dose 2; N=13, 8, 36) | 1.86 (0.89 to 3.88) | 65 (25 to 165) | 47 (31 to 72) | |
| M10713 strain (dose 1; N=13, 7, 38) | 35 (18 to 68) | 30 (12 to 74) | 11 (6.7 to 19) | |
| M10713 strain (dose 2; N=12, 8, 36) | 21 (9.25 to 47) | 36 (13 to 98) | 33 (22 to 51) | |

Statistical analyses

No statistical analyses for this end point

Secondary: 10) Percentage of subjects with serum bactericidal antibody titers $\geq 1:4$ and $\geq 1:8$ after receiving two booster doses of either rMenB or rMenB+OMV NZ vaccine at 40 & 42 months of age

| | |
|-----------------|---|
| End point title | 10) Percentage of subjects with serum bactericidal antibody titers $\geq 1:4$ and $\geq 1:8$ after receiving two booster doses of either rMenB or rMenB+OMV NZ vaccine at 40 & 42 months of age ^[13] |
|-----------------|---|

End point description:

The percentages of subjects (who had previously received one dose of MenB vaccine in parent study) with hSBA $\geq 1:4$ and $\geq 1:8$, against N.meningitidis B strains after receiving two booster doses of either rMenB or rMenB+OMV NZ vaccine at 40 & 42 months of age are reported.

Analysis was done on the MITT – Booster Response population.

| | |
|--------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| 1 month post vaccination | |

Notes:

[13] - 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: There was no statistical null hypothesis associated with this immunogenicity objective.

| End point values | 3rMenB | 3rMenB+OMV NZ | Naive_4042 | |
|---|-----------------|------------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 13 | 8 | 38 | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| H44/76 strain ($\geq 1:4$ – booster dose 1) | 100 (75 to 100) | 100 (59 to 100) | 89 (75 to 100) | |
| H44/76 strain ($\geq 1:4$ – booster dose 2) | 100 (75 to 100) | 100 (63 to 100) | 100 (90 to 100) | |
| H44/76 strain ($\geq 1:8$ – booster dose 1) | 100 (75 to 100) | 100 (59 to 100) | 63 (46 to 78) | |
| H44/76 strain ($\geq 1:8$ – booster dose 2) | 100 (75 to 100) | 100 (63 to 100) | 100 (90 to 100) | |
| 5/99 strain ($\geq 1:4$ – booster dose 1) | 100 (75 to 100) | 100 (59 to 100) | 76 (60 to 89) | |
| 5/99 strain ($\geq 1:4$ – booster dose 2) | 100 (75 to 100) | 100 (63 to 100) | 100 (90 to 100) | |
| 5/99 strain ($\geq 1:8$ – booster dose 1) | 100 (75 to 100) | 100 (59 to 100) | 71 (54 to 85) | |
| 5/99 strain ($\geq 1:8$ – booster dose 2) | 100 (75 to 100) | 100 (63 to 100) | 100 (90 to 100) | |
| NZ 98/254 strain ($\geq 1:4$ – booster dose 1) | 15 (2 to 45) | 100 (59 to 100) | 66 (49 to 80) | |
| NZ 98/254 strain ($\geq 1:4$ – booster dose 2) | 15 (2 to 45) | 100 (63 to 100) | 94 (81 to 99) | |
| NZ 98/254 strain ($\geq 1:8$ – booster dose 1) | 15 (2 to 45) | 100 (59 to 100) | 58 (41 to 74) | |
| NZ 98/254 strain ($\geq 1:8$ – booster dose 2) | 15 (2 to 45) | 100 (63 to 100) | 94 (81 to 99) | |
| M10713 strain ($\geq 1:4$ – booster dose 1) | 100 (75 to 100) | 86 (42 to 100) | 76 (60 to 89) | |
| M10713 strain ($\geq 1:4$ – booster dose 2) | 83 (52 to 98) | 100 (63 to 100) | 89 (74 to 97) | |
| M10713 strain ($\geq 1:8$ – booster dose 1) | 85 (55 to 98) | 86 (42 to 100) | 61 (43 to 76) | |
| M10713 strain ($\geq 1:8$ – booster dose 2) | 75 (43 to 95) | 100 (63 to 100) | 86 (71 to 95) | |

Statistical analyses

No statistical analyses for this end point

Secondary: 11) Percentage of subjects with 4-fold increase in antibody titers after receiving two booster doses of either rMenB or rMenB+OMV NZ vaccine at 40 & 42 months of age

| | |
|-----------------|---|
| End point title | 11) Percentage of subjects with 4-fold increase in antibody titers after receiving two booster doses of either rMenB or rMenB+OMV NZ vaccine at 40 & 42 months of age ^[14] |
|-----------------|---|

End point description:

The percentages of subjects (who had previously received one dose of MenB vaccine in parent study) displaying 4-fold increase in antibody titers over baseline against N.meningitidis B strains, after receiving two booster doses of either rMenB or rMenB+OMV NZ vaccine at 40 & 42 months of age are reported.

Analysis was done on the MITT – Booster Response population.

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

End point timeframe:

1 month post vaccination

Notes:

[14] - 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: There was no statistical null hypothesis associated with this immunogenicity objective.

| End point values | 3rMenB | 3rMenB+OMV NZ | Naive_4042 | |
|---|-----------------|------------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 13 | 8 | 37 | |
| Units: Percentage of subjects | | | | |
| geometric mean (confidence interval 95%) | | | | |
| H44/76 strain (dose 1; N=13, 7, 37) | 100 (75 to 100) | 86 (42 to 100) | 41 (25 to 58) | |
| 5/99 strain (dose 1; N=13, 7, 37) | 100 (75 to 100) | 100 (59 to 100) | 68 (50 to 82) | |
| NZ 98/254 strain (dose 1; N=13, 7, 37) | 15 (2 to 45) | 100 (59 to 100) | 57 (39 to 73) | |
| M10713 strain (dose 1; N=12, 7, 37) | 58 (28 to 85) | 57 (18 to 90) | 14 (5 to 29) | |
| H44/76 strain (dose 2; N=13, 8, 34) | 100 (75 to 100) | 88 (47 to 100) | 97 (85 to 100) | |
| 5/99 strain (dose 2; N=13, 8, 34) | 100 (75 to 100) | 100 (63 to 100) | 100 (90 to 100) | |
| NZ 98/254 strain (dose 2; N=13, 8, 34) | 15 (2 to 45) | 100 (63 to 100) | 94 (80 to 99) | |
| M10713 strain (dose 2; N=11, 8, 34) | 64 (31 to 89) | 75 (35 to 97) | 53 (35 to 70) | |

Statistical analyses

No statistical analyses for this end point

Secondary: 12) Percentage of subjects with serum bactericidal antibody titers $\geq 1:4$ and $\geq 1:8$ following two catch up doses of rMenB+OMV NZ vaccine given one month apart, either at 40 or 60 months of age

| | |
|-----------------|---|
| End point title | 12) Percentage of subjects with serum bactericidal antibody titers $\geq 1:4$ and $\geq 1:8$ following two catch up doses of rMenB+OMV NZ vaccine given one month apart, either at 40 or 60 months of age ^[15] |
|-----------------|---|

End point description:

The percentages of subjects with hSBA $\geq 1:4$ and $\geq 1:8$ after two catch-up doses of rMenB+OMV NZ vaccine when given either at - 40 & 42 months or 60 & 62 months of age are reported.

Analysis was done on the MITT – Two Dose Catch Up Schedule population.

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

End point timeframe:

1 month post -vaccine dose two

Notes:

[15] - 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: There was no statistical null hypothesis associated with this immunogenicity objective.

| End point values | Naive_4042 | Naive_6062 | | |
|------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 36 | 42 | | |
| Units: Percentages of subjects | | | | |
| number (confidence interval 95%) | | | | |
| H44/76 strain (hSBA \geq 1:4) | 100 (90 to 100) | 93 (81 to 99) | | |
| H44/76 strain (hSBA \geq 1:8) | 100 (90 to 100) | 93 (81 to 99) | | |
| 5/99 strain (hSBA \geq 1:4) | 100 (90 to 100) | 100 (92 to 100) | | |
| 5/99 strain (hSBA \geq 1:8) | 100 (90 to 100) | 100 (92 to 100) | | |
| NZ 98/254 strain (hSBA \geq 1:4) | 94 (81 to 99) | 100 (92 to 100) | | |
| NZ 98/254 strain (hSBA \geq 1:8) | 94 (81 to 99) | 90 (77 to 97) | | |
| M10713 strain (hSBA \geq 1:4) | 89 (74 to 97) | 100 (91 to 100) | | |
| M10713 strain (hSBA \geq 1:8) | 86 (71 to 95) | 98 (87 to 100) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: 13) Geometric mean antibody titers in children after two catch up doses of rMenB+OMV NZ vaccine given, either at 40 or 60 months of age.

| | |
|-----------------|--|
| End point title | 13) Geometric mean antibody titers in children after two catch up doses of rMenB+OMV NZ vaccine given, either at 40 or 60 months of age. ^[16] |
|-----------------|--|

End point description:

The geometric mean antibody titers in children after two catch-up doses of rMenB+OMV NZ vaccine when given either at - 40 & 42 months or 60 & 62 months of age are reported.

Analysis was done on the MITT – Two Dose Catch Up Schedule population.

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

End point timeframe:

1 month post vaccine dose two

Notes:

[16] - 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: There was no statistical null hypothesis associated with this immunogenicity objective.

| End point values | Naive_4042 | Naive_6062 | | |
|--|--------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 36 | 42 | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| H44/76 strain | 88 (63 to 123) | 34 (25 to 47) | | |
| 5/99 strain | 1019 (688 to 1510) | 865 (601 to 1244) | | |
| NZ 98/254 strain | 47 (32 to 69) | 29 (20 to 41) | | |

| | | | | |
|--------------------------|---------------|---------------|--|--|
| M10713 strain (N=36, 41) | 33 (24 to 47) | 43 (31 to 59) | | |
|--------------------------|---------------|---------------|--|--|

Statistical analyses

No statistical analyses for this end point

Secondary: 14) Percentage of subjects with a 4-fold increase in antibody titers after receiving two catch up doses of rMenB+OMV NZ vaccine, either at 40 or 60 months of age

| | |
|-----------------|---|
| End point title | 14) Percentage of subjects with a 4-fold increase in antibody titers after receiving two catch up doses of rMenB+OMV NZ vaccine, either at 40 or 60 months of age ^[17] |
|-----------------|---|

End point description:

The percentages of subjects with four-fold increase in hSBA titers over baseline against N.meningitidis B one month after receiving a two catch-up doses of rMenB+OMV NZ vaccine either at 40 & 42 months or 60 & 62 months of age are reported.

Analysis was done on the MITT – Two Dose Catch Up Schedule population.

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

End point timeframe:

1 month post vaccine dose 2

Notes:

[17] - 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: There was no statistical null hypothesis associated with this immunogenicity objective.

| End point values | Naive_4042 | Naive_6062 | | |
|--------------------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 34 | 38 | | |
| Units: Percentage of subjects | | | | |
| number (confidence interval 95%) | | | | |
| H44/76 strain (% 4 fold increase) | 97 (85 to 100) | 71 (54 to 85) | | |
| 5/99 strain (% 4 fold increase) | 100 (90 to 100) | 100 (91 to 100) | | |
| NZ 98/254 strain (% 4 fold increase) | 94 (80 to 99) | 89 (75 to 97) | | |
| M10713 strain (% 4 fold increase) | 53 (35 to 70) | 21 (10 to 37) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: 15) Persisting geometric mean antibody titers against N.meningitidis B in children at 60 months of age

| | |
|-----------------|--|
| End point title | 15) Persisting geometric mean antibody titers against N.meningitidis B in children at 60 months of age |
|-----------------|--|

End point description:

The persisting GMTs against N.meningitidis B strains in children at 60 months of age who had received

one or two booster doses of either rMenB or rMenB+ OMV NZ vaccine or had received two catch-up doses of rMenB+ OMV NZ vaccine at 40 months of age in the present study are compared with GMTs in vaccine-naïve subjects.

Analysis was done on the MITT – 60 Months of Age Antibody Persistence population.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| 18-20 months after last Men B vaccine; baseline for naïve_6062 | |

| End point values | 5rMenB | 5rMenB+OMV NZ | 3rMenB | 3rMenB+OMV NZ |
|--|---------------------|---------------------|-------------------|------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 24 | 16 | 13 | 5 |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| H44/76 strain (N=24, 16, 13, 5, 28, 46) | 3.13 (1.75 to 5.59) | 4.68 (2.3 to 9.52) | 18 (8.08 to 39) | 13 (3.52 to 45) |
| 5/99 strain (N=23, 16, 13, 5, 28, 46) | 43 (19 to 99) | 136 (51 to 365) | 369 (123 to 1103) | 210 (36 to 1227) |
| NZ 98/254 strain | 1.05 (0.8 to 1.38) | 4.95 (3.54 to 6.92) | 1 (0.69 to 1.45) | 11 (5.93 to 20) |
| M10713 strain (N=22, 16, 12, 5, 27, 46) | 12 (7.22 to 20) | 10 (5.67 to 19) | 12 (5.85 to 24) | 25 (8.47 to 74) |

| End point values | Naive_4042 | Naive_6062 | | |
|--|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 29 | 46 | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| H44/76 strain (N=24, 16, 13, 5, 28, 46) | 12 (6.27 to 23) | 2.98 (1.86 to 4.78) | | |
| 5/99 strain (N=23, 16, 13, 5, 28, 46) | 44 (29 to 67) | 1.14 (0.88 to 1.47) | | |
| NZ 98/254 strain | 2.42 (1.59 to 3.66) | 1.04 (0.96 to 1.14) | | |
| M10713 strain (N=22, 16, 12, 5, 27, 46) | 8.52 (5.09 to 14) | 18 (12 to 28) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: 16) Percentage of subjects with persisting hSBA antibody titers $\geq 1:4$ and $\geq 1:8$ in children at 60 months of age

| | |
|-----------------|---|
| End point title | 16) Percentage of subjects with persisting hSBA antibody titers $\geq 1:4$ and $\geq 1:8$ in children at 60 months of age |
|-----------------|---|

End point description:

The percentage of subjects with persisting hSBA titers $\geq 1:4$ and $\geq 1:8$ at 60 months of age against N.meningitidis B strains after having received one or two booster doses of either rMenB or rMenB+ OMV NZ vaccine or had received two catch-up doses of rMenB+ OMV NZ vaccine at 40 months of age in the present study are reported.

Analysis was done on the MITT – 60 Months of Age Antibody Persistence population.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| 18-20 months after last Men B vaccine; baseline for naïve_6062 | |

| End point values | 5rMenB | 5rMenB+OMV NZ | 3rMenB | 3rMenB+OMV NZ |
|--|-----------------|------------------|-----------------|------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 24 | 16 | 13 | 5 |
| Units: Percentages of subjects | | | | |
| number (confidence interval 95%) | | | | |
| hSBA $\geq 1:4$ (H44/76 strain; N=24, 16, 13, 5, 28, 46) | 46 (26 to 67) | 44 (20 to 70) | 85 (55 to 98) | 80 (28 to 99) |
| hSBA $\geq 1:4$ (5/99 strain; N=23, 16, 13, 5, 28, 46) | 83 (61 to 95) | 88 (62 to 98) | 100 (75 to 100) | 100 (48 to 100) |
| hSBA $\geq 1:4$ (NZ 98/254 strain) | 0 (0 to 14) | 69 (41 to 89) | 0 (0 to 25) | 80 (28 to 99) |
| hSBA $\geq 1:4$ (M10713 strain; N=22, 16, 12, 5, 27, 46) | 77 (55 to 92) | 88 (62 to 98) | 92 (62 to 100) | 100 (48 to 100) |
| hSBA $\geq 1:8$ (H44/76 strain; N=24, 16, 13, 5, 28, 46) | 25 (10 to 47) | 31 (11 to 59) | 77 (46 to 95) | 60 (15 to 95) |
| hSBA $\geq 1:8$ (5/99 strain; N=23, 16, 13, 5, 28, 46) | 74 (52 to 90) | 88 (62 to 98) | 100 (75 to 100) | 100 (48 to 100) |
| hSBA $\geq 1:8$ (NZ 98/254 strain) | 0 (0 to 14) | 31 (11 to 59) | 0 (0 to 25) | 40 (5 to 85) |
| hSBA $\geq 1:8$ (M10713 strain; N=22, 16, 12, 5, 27, 46) | 59 (36 to 79) | 63 (35 to 85) | 67 (35 to 90) | 80 (28 to 99) |

| End point values | Naive_4042 | Naive_6062 | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 29 | 46 | | |
| Units: Percentages of subjects | | | | |
| number (confidence interval 95%) | | | | |
| hSBA $\geq 1:4$ (H44/76 strain; N=24, 16, 13, 5, 28, 46) | 71 (51 to 87) | 33 (20 to 48) | | |
| hSBA $\geq 1:4$ (5/99 strain; N=23, 16, 13, 5, 28, 46) | 100 (88 to 100) | 2 (0.055 to 12) | | |
| hSBA $\geq 1:4$ (NZ 98/254 strain) | 31 (15 to 51) | 2 (0.055 to 12) | | |
| hSBA $\geq 1:4$ (M10713 strain; N=22, 16, 12, 5, 27, 46) | 81 (62 to 94) | 83 (69 to 92) | | |
| hSBA $\geq 1:8$ (H44/76 strain; N=24, 16, 13, 5, 28, 46) | 61 (41 to 78) | 26 (14 to 41) | | |
| hSBA $\geq 1:8$ (5/99 strain; N=23, 16, 13, 5, 28, 46) | 93 (76 to 99) | 2 (0.055 to 12) | | |
| hSBA $\geq 1:8$ (NZ 98/254 strain) | 21 (8 to 40) | 0 (0 to 8) | | |
| hSBA $\geq 1:8$ (M10713 strain; N=22, 16, 12, 5, 27, 46) | 48 (29 to 68) | 70 (54 to 82) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: 17) Persisting geometric mean antibody concentrations against vaccine antigen 287-953 in children (who had previously received 4 doses of MenB vaccine in parent study) at 40 months of age

| | |
|-----------------|---|
| End point title | 17) Persisting geometric mean antibody concentrations against vaccine antigen 287-953 in children (who had previously received 4 doses of MenB vaccine in parent study) at 40 months of age ^[18] |
|-----------------|---|

End point description:

The persisting geometric mean antibody concentrations (GMCs) against vaccine antigen 287-953 in children (at 40 months of age) who had previously received 4 doses of either rMenB or rMen+OMV NZ vaccines in parent study, are compared with the GMCs in vaccine-naïve children. GMCs against vaccine antigen 287-953 were measured using enzyme linked immunosorbent assay (ELISA).

Analysis was done on the MITT – 40 Months of Age Antibody Persistence population.

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

End point timeframe:

28 months after last Men B vaccination; Baseline for Naïve_4042 group

Notes:

[18] - 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: There was no statistical null hypothesis associated with this immunogenicity objective.

| End point values | 5rMenB | 5rMenB+OMV NZ | Naïve_4042 | |
|--|-----------------|-----------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 28 | 17 | 40 | |
| Units: AU/mL | | | | |
| geometric mean (confidence interval 95%) | 82 (59 to 113) | 62 (41 to 94) | 23 (19 to 26) | |

Statistical analyses

No statistical analyses for this end point

Secondary: 18) Persisting geometric mean antibody concentrations against vaccine antigen 287-953 in children (who had previously received 1 dose of MenB vaccine in parent study) at 40 months of age

| | |
|-----------------|--|
| End point title | 18) Persisting geometric mean antibody concentrations against vaccine antigen 287-953 in children (who had previously received 1 dose of MenB vaccine in parent study) at 40 months of age ^[19] |
|-----------------|--|

End point description:

The persisting geometric mean antibody concentrations (GMCs) against vaccine antigen 287-953 in in children (at 40 months of age) who had previously received 1 doses of either rMenB or rMen+OMV NZ vaccines in parent study , are compared with the the GMCs in vaccine-naïve children. GMCs against vaccine antigen 287-953 were measure using enzyme linked immunosorbent assay (ELISA).

Analysis was done on the MITT – 40 Months of Age Antibody Persistence population.

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

End point timeframe:

28 months after last Men B vaccination; baseline for Naïve_4042 group

Notes:

[19] - 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: There was no statistical null hypothesis associated with this immunogenicity objective.

| End point values | 3rMenB | 3rMenB+OMV NZ | Naive_4042 | |
|--|-----------------|------------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 14 | 8 | 38 | |
| Units: AU/mL | | | | |
| geometric mean (confidence interval 95%) | 32 (21 to 49) | 28 (16 to 50) | 23 (19 to 26) | |

Statistical analyses

No statistical analyses for this end point

Secondary: 19) Geometric Mean Antibody Concentrations against vaccine antigen 287-953 in Children (Who Had Previously Received 4doses of MenB Vaccine) After Receiving One Booster Dose of Either rMenB or rMenB+OMV NZ at 40 Months of Age

| | |
|-----------------|--|
| End point title | 19) Geometric Mean Antibody Concentrations against vaccine antigen 287-953 in Children (Who Had Previously Received 4doses of MenB Vaccine) After Receiving One Booster Dose of Either rMenB or rMenB+OMV NZ at 40 Months of Age ^[20] |
|-----------------|--|

End point description:

The GMCs against vaccine antigen 287-953 in children (who had previously received four doses MenB vaccine in parent study) after a single booster dose of either rMenB or rMenB+OMV NZ vaccine given at 40 months of age, are compared with the GMCs following one catch-up dose rMenB+OMV NZ vaccine given at 40 months to vaccine-naïve subjects.

Analysis was done on the MITT – Booster Response population.

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

End point timeframe:

1 month post booster ; 1month post dose for naïve_4042 group

Notes:

[20] - 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: There was no statistical null hypothesis associated with this immunogenicity objective.

| End point values | 5rMenB | 5rMenB+OMV NZ | Naive_4042 | |
|--|---------------------|---------------------|-----------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 28 | 19 | 38 | |
| Units: AU/mL | | | | |
| geometric mean (confidence interval 95%) | 5592 (3900 to 8017) | 3934 (2540 to 6093) | 64 (44 to 94) | |

Statistical analyses

No statistical analyses for this end point

Secondary: 20) Geometric Mean Antibody concentrations against vaccine antigen 287-953 in Children After Receiving Two Booster Doses of Either rMenB or rMenB+OMV NZ at 40 &42 Months of Age

| | |
|-----------------|--|
| End point title | 20) Geometric Mean Antibody concentrations against vaccine antigen 287-953 in Children After Receiving Two Booster Doses of Either rMenB or rMenB+OMV NZ at 40 &42 Months of Age ^[21] |
|-----------------|--|

End point description:

The GMCs against vaccine antigen 287-953 in in children (who had previously received 1 dose of either rMenB or rMen+OMV NZ vaccines in parent study) , are compared with the GMCs in children who received to catch-up doses of rMenB+OMV NZ at 40 & 42 months .

Analysis was done on the MITT - Booster Response population.

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

End point timeframe:

1 month after each booster/ vaccine dose

Notes:

[21] - 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: There was no statistical null hypothesis associated with this immunogenicity objective.

| End point values | 3rMenB | 3rMenB+OMV NZ | Naive_4042 | |
|--|---------------------|---------------------|---------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 13 | 8 | 38 | |
| Units: AU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| after 1st booster/vaccine dose (N=13, N=7, N=38) | 2100 (1100 to 4007) | 1764 (731 to 4256) | 64 (44 to 94) | |
| after 2nd booster/vaccine dose (N=13, N=8, N=36) | 3790 (2265 to 6342) | 3660 (1899 to 7055) | 3464 (2782 to 4313) | |

Statistical analyses

No statistical analyses for this end point

Secondary: 21) Geometric Mean Concentrations against vaccine antigen 287-953 in Children After Two Catch up Doses of rMenB+OMV NZ Vaccine Given Either at 40 or 60 Months of Age

| | |
|--|---|
| End point title | 21) Geometric Mean Concentrations against vaccine antigen 287-953 in Children After Two Catch up Doses of rMenB+OMV NZ Vaccine Given Either at 40 or 60 Months of Age ^[22] |
| End point description: The GMCs against vaccine antigen 287-953 in children after two catch-up doses of rMenB+OMV NZ vaccine when given either at - 40 & 42 months or 60 & 62 months of age are reported. | |
| Analysis was done on the MITT - Booster Response population. | |
| End point type | Secondary |
| End point timeframe: 1 month post vaccine dose two | |

Notes:

[22] - 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: There was no statistical null hypothesis associated with this immunogenicity objective.

| End point values | Naive_4042 | Naive_6062 | | |
|--|---------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 36 | 42 | | |
| Units: AU/mL | | | | |
| geometric mean (confidence interval 95%) | 3464 (2672 to 4489) | 1744 (1372 to 2218) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: 22) Persisting geometric mean concentrations against vaccine antigen 287-953 in children at 60 months of age

| | |
|--|--|
| End point title | 22) Persisting geometric mean concentrations against vaccine antigen 287-953 in children at 60 months of age |
| End point description: The persisting GMCs against vaccine antigen 287-953 in children at 60 months of age who had either received one or two booster doses of either rMenB or rMenB+ OMV NZ vaccine or had received two catch-up doses of rMenB+ OMV NZ vaccine at 40 months of age in the present are compared with GMCs in vaccine-naïve subjects. | |
| Analysis was done on the MITT – 60 Months of Age Antibody Persistence population. | |
| End point type | Secondary |
| End point timeframe: 18-20 months after last Men B vaccine; baseline for naïve_6062 | |

| End point values | 5rMenB | 5rMenB+OMV NZ | 3rMenB | 3rMenB+OMV NZ |
|--|------------------|------------------|------------------|------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 24 | 16 | 13 | 5 |
| Units: AU/mL | | | | |
| geometric mean (confidence interval 95%) | 670 (475 to 945) | 320 (210 to 487) | 280 (175 to 447) | 250 (118 to 532) |

| End point values | Naive_4042 | Naive_6062 | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 28 | 47 | | |
| Units: AU/mL | | | | |
| geometric mean (confidence interval 95%) | 121 (88 to 166) | 25 (20 to 32) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: 23) Number of subjects reporting solicited local and systemic adverse events after a receiving two catch-up doses of rMenB+OMV NZ vaccine either at 40 months or 60 months of age

| | |
|-----------------|---|
| End point title | 23) Number of subjects reporting solicited local and systemic adverse events after a receiving two catch-up doses of rMenB+OMV NZ vaccine either at 40 months or 60 months of age ^[23] |
|-----------------|---|

End point description:

The safety and tolerability of two catch-up doses of rMenB+OMV NZ vaccine when administered either at 40 & 42 months or 60 & 62 months of age in children is assessed in terms of number of subjects with solicited local and systemic reactions following vaccination.

Analysis was done on the MITT – Two Dose Catch Up Schedule population.

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

End point timeframe:

Day 1-7 after any vaccination

Notes:

[23] - 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: There was no statistical null hypothesis associated with this safety objective.

| End point values | Naive_4042 | Naive_6062 | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 42 | 50 | | |
| Units: Number of subjects | | | | |
| Local | 42 | 49 | | |
| Injection-site pain | 41 | 46 | | |
| Injection-site erythema | 42 | 48 | | |
| Injection-site induration | 23 | 29 | | |
| Injection-site swelling | 31 | 27 | | |
| Systemic | 38 | 42 | | |
| Changes in eating habits | 21 | 23 | | |
| Sleepiness | 25 | 23 | | |
| Vomiting | 1 | 8 | | |
| Diarrhea | 7 | 7 | | |
| Irritability | 35 | 31 | | |

| | | | | |
|--|----|----|--|--|
| Headache | 8 | 8 | | |
| Arthralgia | 16 | 16 | | |
| Rash | 2 | 4 | | |
| Fever ($\geq 38^{\circ}\text{C}$) | 7 | 6 | | |
| Other | 31 | 33 | | |
| Antipyretic preventive medication used | 30 | 33 | | |
| Antipyretic treatment medication used | 7 | 7 | | |
| Medically attended fever | 0 | 1 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1-7 after each vaccination for Solicited Adverse; Unsolicited AEs were collected throughout the study period.

Adverse event reporting additional description:

The analyses for the data in this section are from the safety set.

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

Dictionary used

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

| | |
|--------------------|----|
| Dictionary version | 17 |
|--------------------|----|

Reporting groups

| | |
|-----------------------|--------|
| Reporting group title | 5rMenB |
|-----------------------|--------|

Reporting group description:

Subjects who had received four doses of rMenB vaccine (at 2,4,6 and 12 months of age) in the parent study were administered a fifth dose of rMenB vaccine, at 40 months of age in the present study.

| | |
|-----------------------|---------------|
| Reporting group title | 5rMenB+OMV NZ |
|-----------------------|---------------|

Reporting group description:

Subjects who had received four doses of rMenB +OMV NZ vaccine (at 2,4,6 and 12 months of age) in the parent study were administered a fifth dose of rMenB +OMV NZ vaccine, at 40 months of age in the present study.

| | |
|-----------------------|--------|
| Reporting group title | 3rMenB |
|-----------------------|--------|

Reporting group description:

Subjects who had previously received one dose of rMenB vaccine (at 12 months of age) were administered two doses of rMenB vaccine, at 40 and 42 months of age in the present study.

| | |
|-----------------------|---------------|
| Reporting group title | 3rMenB+OMV NZ |
|-----------------------|---------------|

Reporting group description:

Subjects who had previously received one dose of rMenB +OMV NZ vaccine (at 12 months of age) were administered two doses of rMenB +OMV NZ vaccine, at 40 and 42 months of age in the present study.

| | |
|-----------------------|------------|
| Reporting group title | Naive_4042 |
|-----------------------|------------|

Reporting group description:

Vaccine-naïve subjects who received two catch -up doses of rMenB+OMV NZ vaccine at 40 and 42 months of age in the present study.

| | |
|-----------------------|------------|
| Reporting group title | Naive_6062 |
|-----------------------|------------|

Reporting group description:

Vaccine-naïve subjects who received two catch -up doses of rMenB+OMV NZ vaccine at 60 and 62 months of age in the present study.

| Serious adverse events | 5rMenB | 5rMenB+OMV NZ | 3rMenB |
|--|----------------|----------------|----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 1 / 19 (5.26%) | 0 / 14 (0.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) haemangioma | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 19 (0.00%) | 0 / 14 (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 |
| Congenital, familial and genetic disorders | | | |
| cystic lymphangioma | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 19 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| migraine | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 19 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| limphadenitis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 19 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| abdominal pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 19 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| asthma | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 19 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| bronchopneumonia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 1 / 19 (5.26%) | 0 / 14 (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 |

| | | | |
|---|----------------|----------------|----------------|
| oral herpes | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 19 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| urinary tract infection | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 19 (0.00%) | 0 / 14 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | 3rMenB+OMV NZ | Naive_4042 | Naive_6062 |
|---|----------------|----------------|----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 2 / 42 (4.76%) | 2 / 50 (4.00%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| haemangioma | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 42 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Congenital, familial and genetic disorders | | | |
| cystic lymphangioma | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 42 (0.00%) | 0 / 50 (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 |
| Nervous system disorders | | | |
| migraine | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 42 (2.38%) | 0 / 50 (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 |
| Blood and lymphatic system disorders | | | |
| limphadenitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 42 (2.38%) | 0 / 50 (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 |
| Gastrointestinal disorders | | | |

| | | | |
|--|----------------|----------------|----------------|
| abdominal pain | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 42 (2.38%) | 0 / 50 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| asthma | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 42 (0.00%) | 0 / 50 (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 |
| Infections and infestations | | | |
| bronchopneumonia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 42 (0.00%) | 0 / 50 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| oral herpes | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 42 (0.00%) | 1 / 50 (2.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| urinary tract infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 42 (0.00%) | 1 / 50 (2.00%) |
| 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: 5 %

| Non-serious adverse events | 5rMenB | 5rMenB+OMV NZ | 3rMenB |
|--|-------------------|-------------------|-------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 29 / 29 (100.00%) | 19 / 19 (100.00%) | 14 / 14 (100.00%) |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 1 / 19 (5.26%) | 0 / 14 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Heat stroke | | | |

| | | | |
|---|------------------------|-------------------------|-------------------------|
| subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 19 (0.00%) 0 | 0 / 14 (0.00%) 0 |
| Overdose subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 19 (0.00%) 0 | 1 / 14 (7.14%) 1 |
| Nervous system disorders | | | |
| Headache subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 19 (0.00%) 0 | 2 / 14 (14.29%) 2 |
| Lethargy subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 19 (0.00%) 0 | 1 / 14 (7.14%) 1 |
| Somnolence subjects affected / exposed occurrences (all) | 13 / 29 (44.83%) 13 | 12 / 19 (63.16%) 15 | 8 / 14 (57.14%) 11 |
| Blood and lymphatic system disorders | | | |
| Lymphadenitis subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 1 / 19 (5.26%) 1 | 0 / 14 (0.00%) 0 |
| General disorders and administration site conditions | | | |
| Injection site erythema alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 28 / 29 (96.55%) 30 | 19 / 19 (100.00%) 21 | 14 / 14 (100.00%) 28 |
| Hyperpyrexia subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 19 (0.00%) 0 | 1 / 14 (7.14%) 1 |
| Injection site induration alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 14 / 29 (48.28%) 15 | 9 / 19 (47.37%) 9 | 8 / 14 (57.14%) 10 |
| Injection site pain subjects affected / exposed occurrences (all) | 17 / 29 (58.62%) 18 | 14 / 19 (73.68%) 14 | 8 / 14 (57.14%) 10 |
| Injection site swelling alternative assessment type: Systematic | | | |

| | | | |
|--|------------------------|----------------------|-----------------------|
| subjects affected / exposed occurrences (all) | 13 / 29 (44.83%) 14 | 5 / 19 (26.32%) 5 | 9 / 14 (64.29%) 12 |
| Pain subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 19 (0.00%) 0 | 0 / 14 (0.00%) 0 |
| Pyrexia subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 1 / 19 (5.26%) 1 | 7 / 14 (50.00%) 8 |
| Local swelling subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 19 (0.00%) 0 | 0 / 14 (0.00%) 0 |
| Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 19 (0.00%) 0 | 1 / 14 (7.14%) 1 |
| Gastrointestinal disorders Abdominal pain upper subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 0 / 19 (0.00%) 0 | 1 / 14 (7.14%) 2 |
| Constipation subjects affected / exposed occurrences (all) | 2 / 29 (6.90%) 2 | 0 / 19 (0.00%) 0 | 0 / 14 (0.00%) 0 |
| Diarrhoea subjects affected / exposed occurrences (all) | 3 / 29 (10.34%) 3 | 1 / 19 (5.26%) 1 | 3 / 14 (21.43%) 3 |
| Faeces discoloured subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 0 / 19 (0.00%) 0 | 1 / 14 (7.14%) 1 |
| Vomiting subjects affected / exposed occurrences (all) | 1 / 29 (3.45%) 1 | 3 / 19 (15.79%) 3 | 3 / 14 (21.43%) 3 |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 2 / 29 (6.90%) 2 | 0 / 19 (0.00%) 0 | 0 / 14 (0.00%) 0 |
| Oropharyngeal pain | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 29 (0.00%) 0 | 1 / 19 (5.26%) 2 | 0 / 14 (0.00%) 0 |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 19 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all) | 0 | 0 | 1 |
| Eczema | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 19 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all) | 1 | 0 | 1 |
| Rash | | | |
| subjects affected / exposed | 4 / 29 (13.79%) | 0 / 19 (0.00%) | 2 / 14 (14.29%) |
| occurrences (all) | 4 | 0 | 3 |
| Psychiatric disorders | | | |
| Irritability | | | |
| subjects affected / exposed | 14 / 29 (48.28%) | 10 / 19 (52.63%) | 9 / 14 (64.29%) |
| occurrences (all) | 16 | 12 | 11 |
| Eating disorders | | | |
| subjects affected / exposed | 5 / 29 (17.24%) | 10 / 19 (52.63%) | 5 / 14 (35.71%) |
| occurrences (all) | 5 | 15 | 7 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 6 / 19 (31.58%) | 4 / 14 (28.57%) |
| occurrences (all) | 0 | 6 | 4 |
| Infections and infestations | | | |
| Ear infection | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | 1 / 19 (5.26%) | 2 / 14 (14.29%) |
| occurrences (all) | 3 | 1 | 2 |
| Eczema infected | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 19 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all) | 0 | 0 | 1 |
| Fungal skin infection | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 19 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all) | 0 | 0 | 1 |
| Impetigo | | | |

| | | | |
|-----------------------------------|-----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 19 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all) | 2 | 0 | 1 |
| Localised infection | | | |
| subjects affected / exposed | 1 / 29 (3.45%) | 0 / 19 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 3 / 29 (10.34%) | 0 / 19 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 1 / 19 (5.26%) | 0 / 14 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Otitis media | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 1 / 19 (5.26%) | 0 / 14 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 19 (0.00%) | 2 / 14 (14.29%) |
| occurrences (all) | 0 | 0 | 2 |
| Skin infection | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 0 / 19 (0.00%) | 1 / 14 (7.14%) |
| occurrences (all) | 0 | 0 | 1 |
| Tonsillitis | | | |
| subjects affected / exposed | 2 / 29 (6.90%) | 0 / 19 (0.00%) | 0 / 14 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 1 / 19 (5.26%) | 0 / 14 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Varicella | | | |
| subjects affected / exposed | 0 / 29 (0.00%) | 1 / 19 (5.26%) | 1 / 14 (7.14%) |
| occurrences (all) | 0 | 1 | 1 |

| Non-serious adverse events | 3rMenB+OMV NZ | Naive_4042 | Naive_6062 |
|---|-----------------|-------------------|------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 8 / 8 (100.00%) | 42 / 42 (100.00%) | 49 / 50 (98.00%) |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |

| | | | |
|--|-----------------------|-------------------------|------------------------|
| subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 42 (0.00%) 0 | 0 / 50 (0.00%) 0 |
| Heat stroke subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | 0 / 42 (0.00%) 0 | 0 / 50 (0.00%) 0 |
| Overdose subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 42 (0.00%) 0 | 0 / 50 (0.00%) 0 |
| Nervous system disorders Headache subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | 8 / 42 (19.05%) 9 | 8 / 50 (16.00%) 10 |
| Lethargy subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 42 (0.00%) 0 | 0 / 50 (0.00%) 0 |
| Somnolence subjects affected / exposed occurrences (all) | 6 / 8 (75.00%) 7 | 25 / 42 (59.52%) 37 | 23 / 50 (46.00%) 35 |
| Blood and lymphatic system disorders Lymphadenitis subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 42 (0.00%) 0 | 0 / 50 (0.00%) 0 |
| General disorders and administration site conditions Injection site erythema alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 8 / 8 (100.00%) 16 | 42 / 42 (100.00%) 90 | 48 / 50 (96.00%) 97 |
| Hyperpyrexia subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 42 (0.00%) 0 | 0 / 50 (0.00%) 0 |
| Injection site induration alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 6 / 8 (75.00%) 11 | 23 / 42 (54.76%) 36 | 29 / 50 (58.00%) 45 |
| Injection site pain | | | |

| | | | |
|---|-----------------|------------------|------------------|
| subjects affected / exposed | 8 / 8 (100.00%) | 41 / 42 (97.62%) | 46 / 50 (92.00%) |
| occurrences (all) | 15 | 76 | 86 |
| Injection site swelling | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 4 / 8 (50.00%) | 31 / 42 (73.81%) | 27 / 50 (54.00%) |
| occurrences (all) | 6 | 47 | 41 |
| Pain | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 42 (0.00%) | 0 / 50 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 7 / 42 (16.67%) | 6 / 50 (12.00%) |
| occurrences (all) | 0 | 9 | 9 |
| Local swelling | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 42 (0.00%) | 0 / 50 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Ear and labyrinth disorders | | | |
| Ear pain | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 42 (0.00%) | 1 / 50 (2.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrointestinal disorders | | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 42 (0.00%) | 1 / 50 (2.00%) |
| occurrences (all) | 0 | 0 | 1 |
| Constipation | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 42 (0.00%) | 0 / 50 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Diarrhoea | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 8 / 42 (19.05%) | 7 / 50 (14.00%) |
| occurrences (all) | 1 | 8 | 8 |
| Faeces discoloured | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 42 (0.00%) | 0 / 50 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 42 (2.38%) | 8 / 50 (16.00%) |
| occurrences (all) | 0 | 1 | 9 |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|--|-----------------------|------------------------|------------------------|
| Cough subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 1 / 42 (2.38%) 1 | 2 / 50 (4.00%) 2 |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 1 / 42 (2.38%) 1 | 1 / 50 (2.00%) 1 |
| Skin and subcutaneous tissue disorders | | | |
| Alopecia subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 42 (0.00%) 0 | 0 / 50 (0.00%) 0 |
| Eczema subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 42 (0.00%) 0 | 1 / 50 (2.00%) 1 |
| Rash subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | 2 / 42 (4.76%) 3 | 4 / 50 (8.00%) 5 |
| Psychiatric disorders | | | |
| Irritability subjects affected / exposed occurrences (all) | 8 / 8 (100.00%) 10 | 35 / 42 (83.33%) 62 | 31 / 50 (62.00%) 48 |
| Eating disorders subjects affected / exposed occurrences (all) | 4 / 8 (50.00%) 4 | 21 / 42 (50.00%) 32 | 23 / 50 (46.00%) 37 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia alternative assessment type: Systematic subjects affected / exposed occurrences (all) | 4 / 8 (50.00%) 4 | 16 / 42 (38.10%) 24 | 16 / 50 (32.00%) 22 |
| Infections and infestations | | | |
| Ear infection subjects affected / exposed occurrences (all) | 1 / 8 (12.50%) 1 | 4 / 42 (9.52%) 4 | 1 / 50 (2.00%) 1 |
| Eczema infected subjects affected / exposed occurrences (all) | 0 / 8 (0.00%) 0 | 0 / 42 (0.00%) 0 | 0 / 50 (0.00%) 0 |
| Fungal skin infection | | | |

| | | | |
|-----------------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 42 (0.00%) | 0 / 50 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Impetigo | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 42 (2.38%) | 1 / 50 (2.00%) |
| occurrences (all) | 0 | 1 | 1 |
| Localised infection | | | |
| subjects affected / exposed | 1 / 8 (12.50%) | 0 / 42 (0.00%) | 0 / 50 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 42 (2.38%) | 1 / 50 (2.00%) |
| occurrences (all) | 0 | 1 | 1 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 42 (2.38%) | 0 / 50 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Otitis media | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 42 (0.00%) | 0 / 50 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Rhinitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 4 / 42 (9.52%) | 1 / 50 (2.00%) |
| occurrences (all) | 0 | 4 | 1 |
| Skin infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 0 / 42 (0.00%) | 0 / 50 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 42 (2.38%) | 2 / 50 (4.00%) |
| occurrences (all) | 0 | 1 | 3 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 2 / 42 (4.76%) | 0 / 50 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Varicella | | | |
| subjects affected / exposed | 0 / 8 (0.00%) | 1 / 42 (2.38%) | 0 / 50 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported