



Clinical trial results:

A phase III, open, randomized, controlled study to demonstrate the immunogenicity, reactogenicity and safety of GSK Biologicals meningococcal serogroup ACWY conjugate vaccine (GSK134612, MenACWY-TT) co-administered with Infanrix hexa compared to individual administration of each vaccine, in healthy 12-through 23-month-old children

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2006-006680-23 |
| Trial protocol | GR DE AT |
| Global end of trial date | 27 October 2008 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 |
| This version publication date | 11 May 2016 |
| First version publication date | 06 March 2015 |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | 109835 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00508261 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | GlaxoSmithKline Biologicals |
| Sponsor organisation address | Rue de l'Institut 89, Rixensart, Belgium, B-1330 |
| Public contact | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com |
| Scientific contact | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com |

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

| | |
|--|-----------------|
| Analysis stage | Final |
| Date of interim/final analysis | 07 April 2009 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 26 May 2008 |
| Global end of trial reached? | Yes |
| Global end of trial date | 27 October 2008 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

In subjects of the MenACWY-TT + Infanrix hexa and MenACWY-TT groups:

To demonstrate the non-inferiority of the MenACWY-TT conjugate vaccine co-administered with combined DTPa-HBV-IPV/Hib vaccine to the MenACWY-TT conjugate vaccine given alone in terms of serum bactericidal antibodies (rSBA) for *N. meningitidis* serogroups A, C, W-135, and Y.

In subjects of the MenACWY-TT + Infanrix hexa and Infanrix hexa groups:

To demonstrate the non-inferiority of the combined DTPa-HBV-IPV/Hib vaccine co-administered with MenACWY-TT conjugate vaccine to DTPa-HBV-IPV/Hib vaccine given alone in terms of geometric mean concentrations (GMCs) of antibodies to pertussis toxoid (PT), filamentous haemagglutinin (FHA), pertactin (PRN), percentages of subjects with antibody concentrations to PRP $\geq 1.0\mu\text{g/ml}$ and to HBsAg $\geq 10\text{mIU/ml}$.

Protection of trial subjects:

All subjects were supervised for 30 min after vaccination/product administration with appropriate medical treatment readily available. Vaccines/products were administered by qualified and trained personnel. Vaccines/products were administered only to eligible subjects that had no contraindications to any components of the vaccines/products. Subjects were followed-up for 30 days after the last vaccination/product administration.

Background therapy: -

Evidence for comparator: -

| | |
|---|----------------|
| Actual start date of recruitment | 01 August 2007 |
| 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 | Austria: 120 |
| Country: Number of subjects enrolled | Germany: 598 |
| Country: Number of subjects enrolled | Greece: 75 |
| Worldwide total number of subjects | 793 |
| EEA total number of subjects | 793 |

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) | 793 |
| Children (2-11 years) | 0 |
| 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: -

Pre-assignment

Screening details:

During the screening the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical history of the subjects and signing informed consent forms.

Period 1

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

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|------------------|--------------------------------|
| Arm title | Nimenrix + Infanrix-hexa Group |
|------------------|--------------------------------|

Arm description: -

| | |
|--|-------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Nimenrix™ |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Single dose intramuscular injection into the left thigh at Day 0.

| | |
|--|-------------------|
| Investigational medicinal product name | Infanrix™ Hexa |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Single dose intramuscular injection into the right thigh at Day 0.

| | |
|------------------|----------------|
| Arm title | Nimenrix Group |
|------------------|----------------|

Arm description: -

| | |
|--|-------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Nimenrix™ |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Single dose intramuscular injection into the left thigh at Day 0.

| | |
|--|-------------------|
| Investigational medicinal product name | Infanrix-hexa™ |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Single dose intramuscular injection into the right thigh at Month 1.

| | |
|--|---------------------|
| Arm title | Infanrix-Hexa Group |
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | Infanrix-hexa™ |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Single dose intramuscular injection into the right thigh at Day 0.

| | |
|--|-------------------|
| Investigational medicinal product name | Nimenrix™ |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Single dose intramuscular injection into the left thigh at Month 1.

| | |
|--|-------------------|
| Arm title | Meningitec Group |
| Arm description: - | |
| Arm type | Active comparator |
| Investigational medicinal product name | Meningitec™ |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

Single dose intramuscular injection into the left thigh at Day 0.

| Number of subjects in period 1 | Nimenrix + Infanrix-hexa Group | Nimenrix Group | Infanrix-Hexa Group |
|---------------------------------------|--------------------------------|----------------|---------------------|
| Started | 222 | 220 | 224 |
| Completed | 219 | 212 | 218 |
| Not completed | 3 | 8 | 6 |
| Consent withdrawn by subject | 3 | 4 | 4 |
| 'Migrated/moved from study area ' | - | 1 | - |
| Others | - | 1 | 1 |
| Lost to follow-up | - | 1 | 1 |
| Serious Adverse Event | - | 1 | - |

| | |
|---------------------------------------|------------------|
| Number of subjects in period 1 | Meningitec Group |
| Started | 127 |

| | |
|-----------------------------------|-----|
| Completed | 126 |
| Not completed | 1 |
| Consent withdrawn by subject | - |
| 'Migrated/moved from study area ' | - |
| Others | - |
| Lost to follow-up | 1 |
| Serious Adverse Event | - |

Baseline characteristics

Reporting groups

| | |
|--------------------------------|--------------------------------|
| Reporting group title | Nimenrix + Infanrix-hexa Group |
| Reporting group description: - | |
| Reporting group title | Nimenrix Group |
| Reporting group description: - | |
| Reporting group title | Infanrix-Hexa Group |
| Reporting group description: - | |
| Reporting group title | Meningitec Group |
| Reporting group description: - | |

| Reporting group values | Nimenrix + Infanrix-hexa Group | Nimenrix Group | Infanrix-Hexa Group |
|---|--------------------------------|----------------|---------------------|
| Number of subjects | 222 | 220 | 224 |
| Age categorical Units: Subjects | | | |
| In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over | | | |
| Age continuous Units: years | | | |
| arithmetic mean | 14.6 | 15 | 14.9 |
| standard deviation | ± 3.01 | ± 3.33 | ± 3.17 |
| Gender categorical Units: Subjects | | | |
| Female | 109 | 106 | 119 |
| Male | 113 | 114 | 105 |

| Reporting group values | Meningitec Group | Total | |
|--|------------------|---------------------------------|--|
| Number of subjects | 127 | 793 | |
| Age categorical Units: Subjects | | | |
| In utero Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years | | 0 0 0 0 0 0 0 | |

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

| | | | |
|--------------------|--------|-----|--|
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 14.6 | | |
| standard deviation | ± 2.99 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 61 | 395 | |
| Male | 66 | 398 | |

End points

End points reporting groups

| | |
|--------------------------------|--------------------------------|
| Reporting group title | Nimenrix + Infanrix-hexa Group |
| Reporting group description: - | |
| Reporting group title | Nimenrix Group |
| Reporting group description: - | |
| Reporting group title | Infanrix-Hexa Group |
| Reporting group description: - | |
| Reporting group title | Meningitec Group |
| Reporting group description: - | |

Primary: Number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY titers $\geq 1:8$.

| | |
|-----------------|--|
| End point title | Number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY titers $\geq 1:8$. ^[1] |
|-----------------|--|

End point description:

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

End point timeframe:

At 1 month after vaccination with Nimenrix vaccine (Month 1)

Notes:

[1] - 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: The analysis was based only on subjects receiving Nimenrix vaccination at Day 0.

| End point values | Nimenrix + Infanrix-hexa Group | Nimenrix Group | | |
|--------------------------------|--------------------------------------|-------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 193 | 186 | | |
| Units: Subjects | | | | |
| rSBA-MenA, M1 (N=193; 183) | 193 | 180 | | |
| rSBA-MenC, M1 (N=191; 183) | 191 | 178 | | |
| rSBA-MenW-135, M1 (N=193; 186) | 193 | 183 | | |
| rSBA-MenY, M1 (N=192, 185) | 192 | 180 | | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Difference in subjects with rSBA-MenA titres $\geq 1:8$ |
|----------------------------|---|

Statistical analysis description:

To demonstrate the non-inferiority of the Nimenrix vaccine co-administered with combined Infanrix-hexa vaccine to the Nimenrix vaccine given alone in terms of bactericidal antibodies to *Neisseria meningitidis* serogroups A, C, W-135, and Y.

| | |
|-------------------|---|
| Comparison groups | Nimenrix + Infanrix-hexa Group v Nimenrix Group |
|-------------------|---|

| | |
|---|--------------------------------|
| Number of subjects included in analysis | 379 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[2] |
| Parameter estimate | Difference in percentages |
| Point estimate | 1.64 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.33 |
| upper limit | 4.71 |

Notes:

[2] - Criterion for non-inferiority:

The lower limit of the two-sided standardized asymptotic 95% confidence interval (CI) for the group difference in the percentages of subjects with serum bactericidal antibodies using baby rabbit complement (rSBA) titer $\geq 1:8$ is greater than or equal to the pre-defined clinical limit of -10%.

| | |
|-----------------------------------|---|
| Statistical analysis title | Difference in subjects with rSAB-MenC titres $\geq 1:8$ |
|-----------------------------------|---|

Statistical analysis description:

To demonstrate the non-inferiority of the Nimenrix vaccine co-administered with combined Infanrix hexa vaccine to the Nimenrix vaccine given alone in terms of bactericidal antibodies to *Neisseria meningitidis* serogroups A, C, W-135, and Y.

| | |
|---|---|
| Comparison groups | Nimenrix + Infanrix-hexa Group v Nimenrix Group |
| Number of subjects included in analysis | 379 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[3] |
| Parameter estimate | Difference in percentages |
| Point estimate | 2.73 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.73 |
| upper limit | 6.24 |

Notes:

[3] - Criterion for non-inferiority:

The lower limit of the two-sided standardized asymptotic 95% confidence interval (CI) for the group difference in the percentages of subjects with serum bactericidal antibodies using baby rabbit complement (rSBA) titer $\geq 1:8$ is greater than or equal to the pre-defined clinical limit of -10%.

| | |
|-----------------------------------|---|
| Statistical analysis title | Difference in subjects with rSAB-MenW titres $\geq 1:8$ |
|-----------------------------------|---|

Statistical analysis description:

To demonstrate the non-inferiority of the Nimenrix vaccine co-administered with combined Infanrix hexa vaccine to the Nimenrix vaccine given alone in terms of bactericidal antibodies to *Neisseria meningitidis* serogroups A, C, W-135, and Y.

| | |
|---|---|
| Comparison groups | Nimenrix + Infanrix-hexa Group v Nimenrix Group |
| Number of subjects included in analysis | 379 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[4] |
| Parameter estimate | Difference in percentages |
| Point estimate | 1.61 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -0.36 |
| upper limit | 4.64 |

Notes:

[4] - Criterion for non-inferiority:

The lower limit of the two-sided standardized asymptotic 95% confidence interval (CI) for the group difference in the percentages of subjects with serum bactericidal antibodies using baby rabbit complement (rSBA) titer $\geq 1:8$ is greater than or equal to the pre-defined clinical limit of -10%.

| | |
|--|---|
| Statistical analysis title | Difference in subjects with rSAB-MenY titres $\geq 1:8$ |
| Statistical analysis description: | |
| To demonstrate the non-inferiority of the Nimenrix vaccine co-administered with combined Infanrix hexa vaccine to the Nimenrix vaccine given alone in terms of bactericidal antibodies to <i>Neisseria meningitidis</i> serogroups A, C, W-135, and Y. | |
| Comparison groups | Nimenrix + Infanrix-hexa Group v Nimenrix Group |
| Number of subjects included in analysis | 379 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[5] |
| Parameter estimate | Difference in percentages |
| Point estimate | 2.7 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.71 |
| upper limit | 6.18 |

Notes:

[5] - Criterion for non-inferiority:

The lower limit of the two-sided standardized asymptotic 95% confidence interval (CI) for the group difference in the percentages of subjects with serum bactericidal antibodies using baby rabbit complement (rSBA) titer $\geq 1:8$ is greater than or equal to the pre-defined clinical limit of -10%.

Primary: Anti-PT, anti-FHA and anti-PRN concentrations

| | |
|--|--|
| End point title | Anti-PT, anti-FHA and anti-PRN concentrations ^[6] |
| End point description: | |
| End point type | Primary |
| End point timeframe: | |
| At 1 month after the first vaccination (Month 1) | |

Notes:

[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: The analysis was based only on subjects receiving Infanrix-hexa vaccination.

| End point values | Nimenrix + Infanrix-hexa Group | Infanrix-Hexa Group | | |
|--|--------------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 191 | 179 | | |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PT, M1 (N=191; 178) | 86 (77 to 95) | 85 (75 to 96) | | |
| Anti-FHA, M1 (N=191; 178) | 542 (492 to 597) | 544 (485 to 611) | | |
| Anti-PRN, M1 (N=190; 179) | 470 (411 to 537) | 450 (387 to 522) | | |

Statistical analyses

| | |
|---|--|
| Statistical analysis title | GMC ratio for anti-PT concentrations |
| Statistical analysis description: To demonstrate the non-inferiority of the combined Infanrix hexa vaccine co-administered with Nimenrix vaccine to Infanrix hexa vaccine given alone in terms of geometric mean concentrations (GMCs) of antibodies to pertussis toxoid (PT) ≥ 1.0 g/mL. | |
| Comparison groups | Nimenrix + Infanrix-hexa Group v Infanrix-Hexa Group |
| Number of subjects included in analysis | 370 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[7] |
| Parameter estimate | Adjusted GMC ratios |
| Point estimate | 0.97 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.83 |
| upper limit | 1.12 |

Notes:

[7] - Criterion for non-inferiority (1 month after the first study vaccination):

The lower limit of the two-sided 95% CI on the GMC ratio for anti-PT (ELISA) is greater than or equal to a pre-defined clinical limit of $\delta = 0.67$.

| | |
|--|--|
| Statistical analysis title | GMC ratio for anti-FHA concentrations |
| Statistical analysis description: To demonstrate the non-inferiority of the combined Infanrix hexa vaccine co-administered with Nimenrix vaccine to Infanrix hexa vaccine given alone in terms of geometric mean concentrations (GMCs) of antibodies to filamentous haemagglutinin (FHA) ≥ 1.0 g/mL. | |
| Comparison groups | Nimenrix + Infanrix-hexa Group v Infanrix-Hexa Group |
| Number of subjects included in analysis | 370 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[8] |
| Parameter estimate | Adjusted GMC ratios |
| Point estimate | 0.98 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.85 |
| upper limit | 1.13 |

Notes:

[8] - Criterion for non-inferiority (1 month after the first study vaccination):

The lower limit of the two-sided 95% CI on the GMC ratio for anti-FHA (ELISA) is greater than or equal to a pre-defined clinical limit of $\delta = 0.67$.

| | |
|-----------------------------------|---------------------------------------|
| Statistical analysis title | GMC ratio for anti-PRN concentrations |
|-----------------------------------|---------------------------------------|

Statistical analysis description:

To demonstrate the non-inferiority of the combined Infanrix hexa vaccine co-administered with Nimenrix

vaccine to Infanrix hexa vaccine given alone in terms of geometric mean concentrations (GMCs) of antibodies to pertactin (PRN) ≥ 1.0 g/mL.

| | |
|---|--|
| Comparison groups | Nimenrix + Infanrix-hexa Group v Infanrix-Hexa Group |
| Number of subjects included in analysis | 370 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[9] |
| Parameter estimate | Adjusted GMC ratios |
| Point estimate | 0.92 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 0.78 |
| upper limit | 1.1 |

Notes:

[9] - Criterion for non-inferiority (1 month after the first study vaccination):

The lower limit of the two-sided 95% CI on the GMC ratio for anti-PRN (ELISA) is greater than or equal to a pre-defined clinical limit of $\delta = 0.67$.

Primary: Number of subjects with anti-HBs concentrations ≥ 10 mIU/mL

| | |
|-----------------|---|
| End point title | Number of subjects with anti-HBs concentrations ≥ 10 |
|-----------------|---|

End point description:

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

End point timeframe:

At 1 month after vaccination with Nimenrix vaccine (Month 1)

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: The analysis was based only on subjects receiving Infanrix-hexa vaccination.

| End point values | Nimenrix + Infanrix-hexa Group | Infanrix-Hexa Group | | |
|-----------------------------|--------------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 181 | 169 | | |
| Units: Subjects | | | | |
| Anti-PT, M1 (N=181; 169) | 180 | 166 | | |

Statistical analyses

| | |
|----------------------------|---|
| Statistical analysis title | Difference in subjects with anti-HBs ≥ 10 mIU/mL |
|----------------------------|---|

Statistical analysis description:

To demonstrate the non-inferiority of the combined Infanrix hexa vaccine co-administered with Nimenrix vaccine to Infanrix hexa vaccine given alone in terms of geometric mean concentrations (GMCs) of antibodies to hepatitis B surface antigen (HBsAg) ≥ 1.0 g/mL.

| | |
|-------------------|--|
| Comparison groups | Nimenrix + Infanrix-hexa Group v Infanrix-Hexa Group |
|-------------------|--|

| | |
|---|---------------------------------|
| Number of subjects included in analysis | 350 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[11] |
| Parameter estimate | Difference in percentages |
| Point estimate | 1.22 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.47 |
| upper limit | 4.6 |

Notes:

[11] - Criterion for non-inferiority (1 month after the first study vaccination):

The lower limit of the two-sided standardized asymptotic 95% CI for the group difference in the percentages of subjects with anti-HBs antibody concentrations ≥ 10 mIU/ml is greater than or equal to the pre-defined clinical limit of -10%.

Primary: Number of subjects with anti-PRP concentrations $\geq 1\mu\text{g/mL}$

| | |
|-----------------|--|
| End point title | Number of subjects with anti-PRP concentrations $\geq 1\mu\text{g/mL}$ ^[12] |
|-----------------|--|

End point description:

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

End point timeframe:

At 1 month after vaccination with Nimenrix vaccine (Month 1)

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: The analysis was based only on subjects receiving Infanrix-hexa vaccination.

| End point values | Nimenrix + Infanrix-hexa Group | Infanrix-Hexa Group | | |
|-----------------------------|--------------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 184 | 173 | | |
| Units: Subjects | | | | |
| Anti-PRP, M1 (N=184; 173) | 183 | 170 | | |

Statistical analyses

| | |
|----------------------------|--|
| Statistical analysis title | Difference in subjects with anti-PRP $\geq 1.0 \mu\text{g/mL}$ |
|----------------------------|--|

Statistical analysis description:

To demonstrate the non-inferiority of the combined Infanrix hexa vaccine co-administered with Nimenrix vaccine to Infanrix hexa vaccine given alone in terms of geometric mean concentrations (GMCs) of antibodies to polyribosyl-ribitol-phosphate (PRP) $\geq 1.0 \mu\text{g/mL}$

| | |
|---|--|
| Comparison groups | Nimenrix + Infanrix-hexa Group v Infanrix-Hexa Group |
| Number of subjects included in analysis | 357 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority ^[13] |
| Parameter estimate | Difference in percentages |
| Point estimate | 1.19 |

| | |
|---------------------|---------|
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.45 |
| upper limit | 4.5 |

Notes:

[13] - Criterion for non-inferiority (1 month after the first study vaccination):

The lower limit of the two-sided standardized asymptotic 95% CI for the group difference in the percentage of subjects with anti-PRP concentrations (ELISA) ≥ 1.0 µg/mL is greater than or equal to the pre-defined clinical limit of -10%.

Secondary: Number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY titers $\geq 1:8$ and $\geq 1:128$

| | |
|-----------------|--|
| End point title | Number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY titers $\geq 1:8$ and $\geq 1:128$ |
|-----------------|--|

End point description:

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

End point timeframe:

At month 0, 1 and 2

| End point values | Nimenrix + Infanrix-hexa Group | Nimenrix Group | Infanrix-Hexa Group | Meningitec Group |
|--|--------------------------------------|-------------------|------------------------|---------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 193 | 186 | 179 | 114 |
| Units: Subjects | | | | |
| rSBA-MenA [M 0], $\geq 1:8$ (N=84,77,72,46) | 30 | 32 | 34 | 18 |
| rSBA-MenA [M 1], $\geq 1:8$ (N=193,183,163,100) | 193 | 180 | 71 | 43 |
| rSBA-MenA [M 2], $\geq 1:8$ (N=0,90,178,0) | 0 | 90 | 178 | 0 |
| rSBA-MenA [M 0], $\geq 1:128$ (N=84,77,72,46) | 18 | 21 | 24 | 11 |
| rSBA-MenA [M 1], $\geq 1:128$ (N=193,183,163,100) | 193 | 179 | 57 | 30 |
| rSBA-MenA [M 2], $\geq 1:128$ (N=0,90,178,0) | 0 | 90 | 178 | 0 |
| rSBA-MenC [M 0], $\geq 1:8$ (N=93,91,92,54) | 20 | 25 | 13 | 11 |
| rSBA-MenC [M 1], $\geq 1:8$ (N=191,183,177,114) | 191 | 178 | 34 | 112 |
| rSBA-MenC [M 2], $\geq 1:8$ (N=0,94,178,0) | 0 | 91 | 178 | 0 |
| rSBA-MenC [M 0], $\geq 1:128$ (N=93,91,92,54) | 5 | 8 | 5 | 3 |
| rSBA-MenC [M 1], $\geq 1:128$ (N=191,183,177,114) | 189 | 172 | 14 | 102 |
| rSBA-MenC [M 2], $\geq 1:128$ (N=0,94,178,0) | 0 | 85 | 157 | 0 |
| rSBA-MenW-135 [M 0], $\geq 1:8$ (N=91,84,85,55) | 43 | 42 | 46 | 22 |
| rSBA-MenW-135 [M 1], $\geq 1:8$ (N=193,186,173,112) | 193 | 183 | 86 | 41 |
| rSBA-MenW-135 [M 2], $\geq 1:8$ (N=0,91,179,0) | 0 | 91 | 179 | 0 |

| | | | | |
|--|-----|-----|-----|----|
| rSBA-MenW-135 [M 0], $\geq 1:128$ (N=91,84,85,55) | 17 | 11 | 23 | 10 |
| rSBA-MenW-135 [M 1], $\geq 1:128$ (N=193,186,173,112) | 193 | 180 | 49 | 23 |
| rSBA-MenW-135 [M 2], $\geq 1:128$ (N=0,91,179,0) | 0 | 90 | 178 | 0 |
| rSBA-MenY [M 0], $\geq 1:8$ (N=94,87,87,55) | 57 | 53 | 53 | 30 |
| rSBA-MenY [M 1], $\geq 1:8$ (N=192,185,174,110) | 192 | 180 | 103 | 71 |
| rSBA-MenY [M 2], $\geq 1:8$ (N=0,92,179,0) | 0 | 91 | 178 | 0 |
| rSBA-MenY [M 0], $\geq 1:128$ (N=94,87,87,55) | 38 | 37 | 34 | 20 |
| rSBA-MenY [M 1], $\geq 1:128$ (N=192,185,174,110) | 192 | 178 | 79 | 38 |
| rSBA-MenY [M 2], $\geq 1:128$ (N=0,92,179,0) | 0 | 91 | 178 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY titers

| | |
|------------------------|--|
| End point title | rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY titers |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| At month 0, 1 and 2 | |

| End point values | Nimenrix + Infanrix-hexa Group | Nimenrix Group | Infanrix-Hexa Group | Meningitec Group |
|---|--------------------------------------|---------------------------|---------------------------|------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 193 | 186 | 179 | 114 |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| rSBA-MenA [M 0], (N=84,77,72,46) | 15 (10 to 22.4) | 19 (12.2 to 29.5) | 24 (15 to 38.4) | 15.9 (9.2 to 27.5) |
| rSBA-MenA [M 1], (N=193,183,163,100) | 3152.9 (2752.5 to 3611.4) | 3169.9 (2577.2 to 3898.8) | 24.2 (17.4 to 33.7) | 21.5 (14.5 to 32.1) |
| rSBA-MenA [M 2], (N=0,90,178,0) | 0 (0 to 0) | 2881.9 (2292 to 3623.6) | 1938.3 (1699.1 to 2211.2) | 0 (0 to 0) |
| rSBA-MenC [M 0], (N=93,91,92,54) | 7.4 (5.7 to 9.6) | 9.1 (6.7 to 12.2) | 6.1 (4.9 to 7.7) | 7.6 (5.2 to 11.2) |
| rSBA-MenC [M 1], (N=191,183,177,114) | 879.7 (763.1 to 1014) | 828.7 (672.4 to 1021.4) | 7.5 (6.1 to 9.3) | 691.4 (520.8 to 917.9) |
| rSBA-MenC [M 2], (N=0,94,178,0) | 0 (0 to 0) | 519.6 (391.7 to 689.2) | 386 (333.9 to 446.2) | 0 (0 to 0) |

| | | | | |
|---|---------------------------|---------------------------|---------------------------|---------------------|
| rSBA-MenW-135 [M 0], (N=91,84,85,55) | 19 (13.1 to 27.6) | 19.2 (13.3 to 27.7) | 24.8 (16.7 to 36.8) | 15.6 (9.8 to 25) |
| rSBA-MenW-135 [M 1], (N=193,186,173,112) | 4147 (3670.1 to 4685.8) | 4022.3 (3269.2 to 4948.8) | 25.2 (18.6 to 34.2) | 14.2 (10.2 to 19.7) |
| rSBA-MenW-135 [M 2], (N=0,91,179,0) | 0 (0 to 0) | 3630.1 (2899.1 to 4545.4) | 2466.4 (2175.4 to 2796.4) | 0 (0 to 0) |
| rSBA-MenY [M 0], (N=94,87,87,55) | 36.8 (24.7 to 54.8) | 45.4 (29.1 to 71) | 41.2 (26.7 to 63.4) | 32 (18.3 to 55.9) |
| rSBA-MenY [M 1], (N=192,185,174,110) | 3461.8 (2990.1 to 4007.9) | 3167.7 (2521.9 to 3978.9) | 45.9 (33 to 63.9) | 47.2 (32.1 to 69.3) |
| rSBA-MenY [M 2], (N=0,92,179,0) | 0 (0 to 0) | 3010.4 (2325.3 to 3897.3) | 2446.9 (2088.5 to 2866.8) | 0 (0 to 0) |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with Anti-polysaccharide A (anti-PSA), anti-PSC, anti-PSW, and anti-PSY $\geq 0.3\mu\text{g/mL}$ and $\geq 2.0\mu\text{g/mL}$

| | |
|-----------------|--|
| End point title | Number of subjects with Anti-polysaccharide A (anti-PSA), anti-PSC, anti-PSW, and anti-PSY $\geq 0.3\mu\text{g/mL}$ and $\geq 2.0\mu\text{g/mL}$ |
|-----------------|--|

End point description:

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

End point timeframe:

At month 0, 1 and 2

| End point values | Nimenrix + Infanrix-hexa Group | Nimenrix Group | Infanrix-Hexa Group | Meningitec Group |
|---|--------------------------------------|-------------------|------------------------|---------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 51 | 47 | 47 | 29 |
| Units: Subjects | | | | |
| Anti-PSA [Month 0], ≥ 0.3 (N=45,45,41,27) | 4 | 1 | 1 | 1 |
| Anti-PSA [Month 1], ≥ 0.3 (N=46,46,37,25) | 46 | 45 | 1 | 1 |
| Anti-PSA [Month 2], ≥ 0.3 (N=0,44,42,0) | 0 | 44 | 42 | 0 |
| Anti-PSA [Month 0], ≥ 2.0 (N=45,45,41,27) | 0 | 0 | 0 | 0 |
| Anti-PSA [Month 1], ≥ 2.0 (N=45,45,41,27) | 46 | 44 | 1 | 0 |
| Anti-PSA [Month 2], ≥ 2.0 (N=45,45,41,27) | 0 | 43 | 40 | 0 |
| Anti-PSC [Month 0], ≥ 0.3 (N=48,43,46,29) | 1 | 1 | 2 | 0 |
| Anti-PSC [Month 1], ≥ 0.3 (N=51,41,47,28) | 51 | 41 | 2 | 28 |

| | | | | |
|---|----|----|----|----|
| Anti-PSC [Month 2], ≥ 0.3 (N=0,41,47,0) | 0 | 41 | 47 | 0 |
| Anti-PSC [Month 0], ≥ 2.0 (N=48,43,46,29) | 1 | 0 | 0 | 0 |
| Anti-PSC [Month 1], ≥ 2.0 (N=51,41,47,28) | 50 | 41 | 0 | 26 |
| Anti-PSC [Month 2], ≥ 2.0 (N=0,41,47,0) | 0 | 41 | 43 | 0 |
| Anti-PSW-135 [Month 0], ≥ 0.3 (N=44,43,40,26) | 1 | 1 | 2 | 0 |
| Anti-PSW-135 [Month 1], ≥ 0.3 (N=44,47,41,26) | 44 | 43 | 2 | 0 |
| Anti-PSW-135 [Month 2], ≥ 0.3 (N=0,44,41,0) | 0 | 43 | 41 | 0 |
| Anti-PSW-135 [Month 0], ≥ 2.0 (N=44,43,40,26) | 0 | 0 | 1 | 0 |
| Anti-PSW-135 [Month 1], ≥ 2.0 (N=44,47,41,26) | 40 | 39 | 2 | 0 |
| Anti-PSW-135 [Month 2], ≥ 2.0 (N=0,41,41,0) | 0 | 36 | 29 | 0 |
| Anti-PSY [Month 0], ≥ 0.3 (N=45,44,42,29) | 1 | 1 | 0 | 0 |
| Anti-PSY [Month 1], ≥ 0.3 (N=45,45,37,23) | 45 | 43 | 1 | 0 |
| Anti-PSY [Month 2], ≥ 0.3 (N=0,44,41,0) | 0 | 44 | 41 | 0 |
| Anti-PSY [Month 0], ≥ 2.0 (N=45,44,42,29) | 0 | 0 | 0 | 0 |
| Anti-PSY [Month 1], ≥ 2.0 (N=45,45,37,23) | 40 | 42 | 1 | 0 |
| Anti-PSY [Month 2], ≥ 2.0 (N=0,44,41,0) | 0 | 40 | 34 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-polysaccharide A (anti-PSA), anti-PSC, anti-PSW, and anti-PSY antibody concentrations

| | |
|-----------------|--|
| End point title | Anti-polysaccharide A (anti-PSA), anti-PSC, anti-PSW, and anti-PSY antibody concentrations |
|-----------------|--|

End point description:

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

End point timeframe:

At month 0, 1 and 2

| End point values | Nimenrix + Infanrix-hexa Group | Nimenrix Group | Infanrix-Hexa Group | Meningitec Group |
|---|--------------------------------------|---------------------------|--------------------------|-------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 48 | 47 | 47 | 29 |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PSA [M 0], (N=45,45,41,27) | 0.17 (0.15 to 0.19) | 0.15 (0.15 to 0.16) | 0.16 (0.14 to 0.18) | 0.16 (0.14 to 0.18) |
| Anti-PSA [M 1], (N=46,46,37,25) | 31.01 (23.73 to 40.52) | 33.15 (21.89 to 50.18) | 0.17 (0.13 to 0.22) | 0.16 (0.14 to 0.18) |
| Anti-PSA [M 2], (N=0,44,42,0) | 0 (0 to 0) | 16.93 (12.39 to 23.13) | 12.28 (9.38 to 16.06) | 0 (0 to 0) |
| Anti-PSC [M 0], (N=48,43,46,29) | 0.16 (0.14 to 0.2) | 0.16 (0.14 to 0.17) | 0.16 (0.15 to 0.17) | 0.15 (0.15 to 0.15) |
| Anti-PSC [M 1], (N=51,41,47,28) | 13.74 (10.68 to 17.67) | 23.52 (18.91 to 29.25) | 0.16 (0.15 to 0.17) | 7.99 (5.57 to 11.46) |
| Anti-PSC [M 2], (N=0,41,47,0) | 0 (0 to 0) | 9.73 (7.82 to 12.12) | 5.84 (4.66 to 7.32) | 0 (0 to 0) |
| Anti-PSW-135 [M 0], (N=44,43,40,26) | 0.16 (0.14 to 0.17) | 0.15 (0.15 to 0.16) | 0.17 (0.14 to 0.22) | 0.15 (0.15 to 0.15) |
| Anti-PSW-135 [M 1], (N=44,47,41,26) | 6.43 (4.92 to 8.4) | 4.15 (2.82 to 6.11) | 0.18 (0.14 to 0.22) | 0.15 (0.15 to 0.15) |
| Anti-PSW-135 [M 2], (N=0,44,41,0) | 0 (0 to 0) | 3.99 (2.91 to 5.48) | 3.4 (2.52 to 4.59) | 0 (0 to 0) |
| Anti-PSY [M 0], (N=45,44,42,29) | 0.15 (0.15 to 0.16) | 0.15 (0.15 to 0.16) | 0.15 (0.15 to 0.15) | 0.15 (0.15 to 0.15) |
| Anti-PSY [M 1], (N=45,45,37,23) | 6.52 (4.91 to 8.65) | 9.42 (6.49 to 13.66) | 0.17 (0.13 to 0.21) | 0.15 (0.15 to 0.15) |
| Anti-PSY [M 2], (N=0,44,41,0) | 0 (0 to 0) | 7.86 (6.04 to 10.23) | 4.76 (3.73 to 6.09) | 0 (0 to 0) |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects for Anti-tetanus toxoid (anti-TT)

| | |
|-----------------|--|
| End point title | Number of seroprotected subjects for Anti-tetanus toxoid (anti-TT) |
|-----------------|--|

End point description:

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

End point timeframe:

At month 0, 1 and 2

| End point values | Nimenrix + Infanrix-hexa Group | Nimenrix Group | Infanrix-Hexa Group | Meningitec Group |
|--|--------------------------------------|-------------------|------------------------|---------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 186 | 180 | 176 | 110 |
| Units: Subjects | | | | |
| anti-TT [M 0], ≥ 0.1 (N=186,177,171,108) | 177 | 161 | 155 | 99 |
| anti-TT [M 1], ≥ 0.1 (N=184,180,174,110) | 184 | 177 | 173 | 99 |
| anti-TT [M 2], ≥ 0.1 (N=0,177,176,0) | 0 | 177 | 176 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-tetanus toxoid (anti-TT) antibody concentrations

| | |
|------------------------|---|
| End point title | Anti-tetanus toxoid (anti-TT) antibody concentrations |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| At month 0, 1 and 2 | |

| End point values | Nimenrix + Infanrix-hexa Group | Nimenrix Group | Infanrix-Hexa Group | Meningitec Group |
|---|--------------------------------------|------------------------------|---------------------------|---------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 186 | 180 | 176 | 110 |
| Units: IU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| anti-TT [M 0], (N=186,177,171,108) | 0.481 (0.417 to 0.554) | 0.39 (0.332 to 0.457) | 0.416 (0.354 to 0.489) | 0.393 (0.325 to 0.475) |
| anti-TT [M 1], (N=184,180,174,110) | 10.47 (9.131 to 12.007) | 7.941 (6.517 to 9.677) | 6.189 (5.404 to 7.089) | 0.374 (0.306 to 0.457) |
| anti-TT [M 2], (N=0,177,176,0) | 0 (0 to 0) | 13.966 (12.199 to 15.987) | 8.236 (7.348 to 9.231) | 0 (0 to 0) |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroprotected for anti-diphtheria (anti-D)

| | |
|-----------------|---|
| End point title | Number of subjects seroprotected for anti-diphtheria (anti-D) |
|-----------------|---|

End point description:

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

End point timeframe:

At month 0, 1 and 2

| End point values | Nimenrix + Infanrix-hexa Group | Nimenrix Group | Infanrix-Hexa Group | Meningitec Group |
|---|--------------------------------------|-------------------|------------------------|---------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 185 | 178 | 176 | 110 |
| Units: Subjects | | | | |
| anti-D [M 0], ≥ 0.1 (N=185,174,170,106) | 169 | 157 | 154 | 94 |
| anti-D [M 1], ≥ 0.1 (N=184,178,174,110) | 184 | 156 | 173 | 109 |
| anti-D [M 2], ≥ 0.1 (N=0,177,176,0) | 0 | 176 | 176 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-diphtheria (anti-D) antibody concentrations

| | |
|-----------------|--|
| End point title | Anti-diphtheria (anti-D) antibody concentrations |
|-----------------|--|

End point description:

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

End point timeframe:

At month 0, 1 and 2

| End point values | Nimenrix + Infanrix-hexa Group | Nimenrix Group | Infanrix-Hexa Group | Meningitec Group |
|---|--------------------------------------|---------------------------|---------------------------|---------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 185 | 178 | 176 | 110 |
| Units: IU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| anti-D [M 0], (N=185,174,170,106) | 0.477 (0.407 to 0.559) | 0.476 (0.397 to 0.57) | 0.437 (0.367 to 0.521) | 0.452 (0.355 to 0.574) |
| anti-D [M 1], (N=184,178,174,110) | 7.636 (6.889 to 8.465) | 0.404 (0.335 to 0.487) | 7.292 (6.362 to 8.358) | 5.201 (4.243 to 6.376) |
| anti-D [M 2], (N=0,177,176,0) | 0 (0 to 0) | 8.561 (7.553 to 9.703) | 5.21 (4.623 to 5.872) | 0 (0 to 0) |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroprotected for anti-polio type 1, 2 & 3

| | |
|-----------------|---|
| End point title | Number of subjects seroprotected for anti-polio type 1, 2 & 3 |
|-----------------|---|

End point description:

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

End point timeframe:

At month 0, 1 and 2

| End point values | Nimenrix + Infanrix-hexa Group | Nimenrix Group | Infanrix-Hexa Group | Meningitec Group |
|-----------------------------------|--------------------------------------|-------------------|------------------------|---------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 168 | 164 | 164 | 100 |
| Units: Subjects | | | | |
| anti-p1 [M 0] (N=168,161,156,100) | 158 | 143 | 142 | 90 |
| anti-p1 [M 1] (N=167,164,164,99) | 166 | 149 | 163 | 89 |
| anti-p1 [M 2] (N=0,160,162,0) | 0 | 159 | 161 | 0 |
| anti-p2 [M 0] (N=168,161,156,98) | 153 | 141 | 145 | 80 |
| anti-p2 [M 1] (N=167,164,163,98) | 166 | 147 | 161 | 80 |
| anti-p2 [M 2] (N=0,159,162,0) | 0 | 159 | 161 | 0 |
| anti-p3 [M 0] (N=168,161,157,100) | 155 | 148 | 143 | 88 |
| anti-p3 [M 1] (N=167,163,163,100) | 167 | 150 | 160 | 87 |
| anti-p3 [M 2] (N=0,160,161,0) | 0 | 159 | 159 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-polio type 1, 2 & 3 titers

| | |
|-----------------|---------------------------------|
| End point title | Anti-polio type 1, 2 & 3 titers |
|-----------------|---------------------------------|

End point description:

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

End point timeframe:

At month 0, 1 and 2

| End point values | Nimenrix + Infanrix-hexa Group | Nimenrix Group | Infanrix-Hexa Group | Meningitec Group |
|---|--------------------------------------|------------------------------|------------------------------|--------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 168 | 164 | 164 | 100 |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| anti-p1 [M 0] (N=168,161,156,100) | 84.2 (67.2 to 105.4) | 72.5 (55.6 to 94.5) | 83.6 (65.5 to 106.6) | 71.7 (51.7 to 99.6) |
| anti-p1 [M 1] (N=167,164,164,99) | 984.4 (830.4 to 1167) | 74.2 (56.7 to 97.3) | 1308.5 (1073.2 to 1595.5) | 66.3 (46.6 to 94.4) |
| anti-p1 [M 2] (N=0,160,162,0) | 0 (0 to 0) | 1288.2 (1052.5 to 1576.6) | 1108.4 (913.5 to 1344.8) | 0 (0 to 0) |
| anti-p2 [M 0] (N=168,161,156,98) | 76.8 (60.8 to 97) | 66.3 (50.9 to 86.5) | 65.6 (51.2 to 84.2) | 49.3 (34.9 to 69.6) |
| anti-p2 [M 1] (N=167,164,163,98) | 1372 (1153.5 to 1631.9) | 70.3 (53.4 to 92.6) | 1540.4 (1253.2 to 1893.2) | 49.8 (34.5 to 71.9) |
| anti-p2 [M 2] (N=0,159,162,0) | 0 (0 to 0) | 1650.5 (1358.5 to 2005.3) | 1174.5 (961.4 to 1434.8) | 0 (0 to 0) |
| anti-p3 [M 0] (N=168,161,157,100) | 104.4 (81.1 to 134.4) | 99.8 (77.5 to 128.5) | 113.2 (86.9 to 147.5) | 102.9 (72.8 to 145.4) |
| anti-p3 [M 1] (N=167,163,163,100) | 2295.6 (1952.1 to 2699.4) | 96.6 (74.2 to 125.8) | 2034.3 (1594.9 to 2594.8) | 85.3 (58.7 to 124.1) |
| anti-p3 [M 2] (N=0,160,161,0) | 0 (0 to 0) | 2478 (2049.2 to 2996.4) | 1655.1 (1308.9 to 2092.9) | 0 (0 to 0) |

Statistical analyses

No statistical analyses for this end point

Secondary: Numbers of seroprotected subjects for anti-PRP

| | |
|------------------------|--|
| End point title | Numbers of seroprotected subjects for anti-PRP |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| At month 0, 1 and 2 | |

| End point values | Nimenrix + Infanrix-hexa Group | Nimenrix Group | Infanrix-Hexa Group | Meningitec Group |
|--|--------------------------------------|-------------------|------------------------|---------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 185 | 179 | 176 | 110 |
| Units: Subjects | | | | |
| anti-PRP [M 0] ≥ 1.0 (N=185,175,171,108) | 73 | 64 | 65 | 36 |
| anti-PRP [M 1] ≥ 1.0 (N=184,179,173,110) | 183 | 70 | 170 | 34 |
| anti-PRP [M 2] ≥ 1.0 (N=0,177,176,0) | 0 | 172 | 170 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PRP antibody concentrations

| | |
|------------------------|----------------------------------|
| End point title | Anti-PRP antibody concentrations |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| At month 0, 1 and 2 | |

| End point values | Nimenrix + Infanrix-hexa Group | Nimenrix Group | Infanrix-Hexa Group | Meningitec Group |
|---|--------------------------------------|------------------------------|------------------------------|---------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 185 | 179 | 176 | 110 |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| anti-PRP [M 0] (N=185,175,171,108) | 0.806 (0.658 to 0.987) | 0.665 (0.528 to 0.839) | 0.766 (0.596 to 0.986) | 0.585 (0.449 to 0.762) |
| anti-PRP [M 1] (N=184,179,173,110) | 25.556 (21.358 to 30.579) | 0.711 (0.56 to 0.904) | 31.165 (25.142 to 38.631) | 0.55 (0.42 to 0.72) |
| anti-PRP [M 2] (N=0,177,176,0) | 0 (0 to 0) | 12.239 (10.392 to 14.414) | 21.023 (17.036 to 25.942) | 0 (0 to 0) |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects for anti-HBs

| | |
|-----------------|---|
| End point title | Number of seroprotected subjects for anti-HBs |
|-----------------|---|

End point description:

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

End point timeframe:

At month 0, 1 and 2

| End point values | Nimenrix + Infanrix-hexa Group | Nimenrix Group | Infanrix-Hexa Group | Meningitec Group |
|--|--------------------------------------|-------------------|------------------------|---------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 181 | 174 | 169 | 106 |
| Units: Subjects | | | | |
| anti-HBS [M 0] ≥ 10 (N=180,169,166,102) | 173 | 158 | 155 | 95 |
| anti-HBS [M 1] ≥ 10 (N=181,174,169,106) | 180 | 160 | 166 | 100 |
| anti-HBS [M 2] ≥ 10 (N=0,173,168,0) | 0 | 172 | 167 | 0 |
| anti-HBS [M 0] ≥ 100 (N=180,169,166,102) | 92 | 80 | 75 | 46 |
| anti-HBS [M 1] ≥ 100 (N=181,174,169,106) | 169 | 85 | 155 | 46 |
| anti-HBS [M 2] ≥ 100 (N=0,173,168,0) | 0 | 168 | 158 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-HBs antibody concentrations

| | |
|-----------------|----------------------------------|
| End point title | Anti-HBs antibody concentrations |
|-----------------|----------------------------------|

End point description:

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

End point timeframe:

At month 0, 1 and 2

| End point values | Nimenrix + Infanrix-hexa Group | Nimenrix Group | Infanrix-Hexa Group | Meningitec Group |
|---|--------------------------------------|-------------------------|--------------------------|-------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 181 | 174 | 169 | 106 |
| Units: mIU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| anti-HBS [M 0] (N=180,169,166,102) | 111.6 (90.9 to 136.9) | 92.8 (75.3 to 114.4) | 101.2 (81.5 to 125.7) | 85.6 (65.7 to 111.5) |

| | | | | |
|------------------------------------|-------------------------|---------------------------|---------------------------|-----------------------|
| anti-HBS [M 1] (N=181,174,169,106) | 2048.4 (1589.3 to 2640) | 95 (74.8 to 120.6) | 1711.6 (1292.7 to 2266.3) | 101.6 (75.5 to 136.7) |
| anti-HBS [M 2] (N=0,173,168,0) | 0 (0 to 0) | 2392.3 (1841.7 to 3107.4) | 1241 (976.2 to 1577.7) | 0 (0 to 0) |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with a vaccine response to PT, FHA and PRN antigens

| | |
|-----------------|--|
| End point title | Number of subjects with a vaccine response to PT, FHA and PRN antigens ^[14] |
|-----------------|--|

End point description:

Vaccine response to these antigens is defined as appearance of antibodies in subjects who were seronegative (antibody concentration < 5 EL.U/mL) at pre-vaccination or as at least a 2-fold increase in post-over pre-vaccination antibody concentrations in subjects seropositive at pre-vaccination.

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

End point timeframe:

At 1 month after 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: The analysis was based only on subjects receiving experimental vaccination.

| End point values | Nimenrix + Infanrix-hexa Group | Nimenrix Group | Infanrix-Hexa Group | |
|-----------------------------|--------------------------------------|-------------------|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 30 | 47 | 44 | |
| Units: Subjects | | | | |
| PT (N=30,47,44) | 30 | 47 | 44 | |
| FHA (N=3,1,1) | 3 | 1 | 1 | |
| PRN (N=13,10,18) | 13 | 10 | 18 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PT, anti-FHA and anti-PRN antibody concentrations

| | |
|-----------------|--|
| End point title | Anti-PT, anti-FHA and anti-PRN antibody concentrations |
|-----------------|--|

End point description:

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

End point timeframe:

At month 0, 1 and 2

| End point values | Nimenrix + Infanrix-hexa Group | Nimenrix Group | Infanrix-Hexa Group | Meningitec Group |
|---|--------------------------------------|---------------------|------------------------|---------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 194 | 188 | 182 | 114 |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-PT [M 0] (N=193,187,182,112) | 11 (10 to 12) | 10 (8 to 11) | 10 (9 to 12) | 11 (9 to 13) |
| Anti-PT [M 1] (N=191,180,178,109) | 86 (77 to 95) | 8 (7 to 9) | 85 (75 to 96) | 9 (7 to 10) |
| Anti-PT [M 2] (N=0,177,179,0) | 0 (0 to 0) | 91 (80 to 102) | 63 (55 to 71) | 0 (0 to 0) |
| Anti-FHA [M 0] (N=193,183,181,111) | 51 (44 to 59) | 55 (46 to 66) | 49 (41 to 57) | 55 (44 to 68) |
| Anti-FHA [M 1] (N=191,183,178,110) | 542 (492 to 597) | 48 (40 to 58) | 544 (485 to 611) | 55 (42 to 71) |
| Anti-FHA [M 2] (N=0,178,176,0) | 0 (0 to 0) | 664 (664 to 750) | 413 (366 to 465) | 0 (0 to 0) |
| Anti-PRN [M 0] (N=194,188,182,114) | 26 (23 to 31) | 26 (22 to 31) | 21 (17 to 24) | 23 (18 to 28) |
| Anti-PRN [M 1] (N=190,184,179,112) | 470 (411 to 537) | 23 (19 to 27) | 450 (387 to 522) | 21 (16 to 26) |
| Anti-PRN [M 2] (N=0,178,178,0) | 0 (0 to 0) | 583 (502 to 676) | 336 (286 to 395) | 0 (0 to 0) |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any and Grade 3 solicited local symptoms post-meningococcal vaccination

| | |
|-----------------|--|
| End point title | Number of subjects reporting any and Grade 3 solicited local symptoms post-meningococcal vaccination |
|-----------------|--|

End point description:

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

End point timeframe:

During the 4-day (Days 0-3) follow-up period after Nimenrix vaccination

| End point values | Nimenrix + Infanrix-hexa Group | Nimenrix Group | Infanrix-Hexa Group | Meningitec Group |
|-----------------------------|--------------------------------------|-------------------|------------------------|---------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 220 | 217 | 219 | 126 |
| Units: Subjects | | | | |
| Any Pain | 49 | 30 | 35 | 16 |
| Grade 3 Pain | 3 | 0 | 1 | 1 |
| Any Redness | 70 | 74 | 56 | 36 |
| Grade 3 Redness | 3 | 8 | 8 | 2 |

| | | | | |
|------------------|----|----|----|----|
| Any Swelling | 42 | 36 | 36 | 23 |
| Grade 3 Swelling | 2 | 3 | 7 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any and Grade 3 solicited local symptoms post-combined diphtheria vaccination

| | |
|-----------------|--|
| End point title | Number of subjects reporting any and Grade 3 solicited local symptoms post-combined diphtheria vaccination ^[15] |
|-----------------|--|

End point description:

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

End point timeframe:

During the 4-day (Days 0-3) follow-up period after Infanrix-hexa vaccination

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: The analysis was based only on subjects receiving combined-diphtheria vaccination.

| End point values | Nimenrix + Infanrix-hexa Group | Nimenrix Group | Infanrix-Hexa Group | |
|-----------------------------|--------------------------------------|-------------------|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 220 | 209 | 221 | |
| Units: Subjects | | | | |
| Any Pain | 60 | 65 | 64 | |
| Grade 3 Pain | 6 | 5 | 10 | |
| Any Redness | 70 | 77 | 99 | |
| Grade 3 Redness | 11 | 14 | 27 | |
| Any Swelling | 48 | 53 | 74 | |
| Grade 3 Swelling | 12 | 14 | 22 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any solicited general symptoms following each dose

| | |
|-----------------|---|
| End point title | Number of subjects reporting any solicited general symptoms following each dose |
|-----------------|---|

End point description:

Subjects in the Nimenrix + Infanrix-hexa Group did not receive a second dose of vaccination.

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

End point timeframe:

During the 4-day (Days 0-3) post-vaccination

| End point values | Nimenrix + Infanrix-hexa Group | Nimenrix Group | Infanrix-Hexa Group | Meningitec Group |
|-----------------------------|--------------------------------------|-------------------|------------------------|---------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 220 | 218 | 221 | 126 |
| Units: Subjects | | | | |
| Drowsiness, D1 | 85 | 56 | 80 | 29 |
| Fever, D1 | 80 | 41 | 71 | 15 |
| Irritability, D1 | 83 | 63 | 75 | 25 |
| Loss of appetite, D1 | 51 | 46 | 51 | 15 |
| Drowsiness, D2 | 0 | 63 | 56 | 0 |
| Fever, D2 | 0 | 60 | 37 | 0 |
| Irritability, D2 | 0 | 75 | 50 | 0 |
| Loss of appetite, D2 | 0 | 54 | 38 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any rash

| | |
|-------------------------|---------------------------------------|
| End point title | Number of subjects reporting any rash |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| During the entire study | |

| End point values | Nimenrix + Infanrix-hexa Group | Nimenrix Group | Infanrix-Hexa Group | Meningitec Group |
|-----------------------------|--------------------------------------|-------------------|------------------------|---------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 222 | 220 | 224 | 127 |
| Units: Subjects | | | | |
| Any rash | 13 | 25 | 22 | 12 |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any new onset of chronic illnesses (NOCIs)

| | |
|-------------------------|---|
| End point title | Number of subjects reporting any new onset of chronic illnesses (NOCIs) |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| During the entire study | |

| End point values | Nimenrix + Infanrix-hexa Group | Nimenrix Group | Infanrix-Hexa Group | Meningitec Group |
|-----------------------------|--------------------------------------|-------------------|------------------------|---------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 222 | 220 | 224 | 127 |
| Units: Subjects | | | | |
| Any NOCIs | 1 | 2 | 6 | 1 |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any conditions prompting emergency room visits (ER)

| | |
|-------------------------|--|
| End point title | Number of subjects reporting any conditions prompting emergency room visits (ER) |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| During the entire study | |

| End point values | Nimenrix + Infanrix-hexa Group | Nimenrix Group | Infanrix-Hexa Group | Meningitec Group |
|-----------------------------|--------------------------------------|-------------------|------------------------|---------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 222 | 220 | 224 | 127 |
| Units: Subjects | | | | |
| Any ER visits | 5 | 3 | 14 | 6 |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited adverse events (AEs) after

the first dose

| | |
|-----------------|--|
| End point title | Number of subjects reporting any unsolicited adverse events (AEs) after the first dose |
|-----------------|--|

End point description:

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

End point timeframe:

Occurring within Day 0-30 following vaccination

| End point values | Nimenrix + Infanrix-hexa Group | Nimenrix Group | Infanrix-Hexa Group | Meningitec Group |
|-----------------------------|--------------------------------------|-------------------|------------------------|---------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 222 | 220 | 224 | 127 |
| Units: Subjects | | | | |
| Any AE(s) | 71 | 81 | 83 | 42 |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited adverse events (AEs) after the second dose

| | |
|-----------------|---|
| End point title | Number of subjects reporting any unsolicited adverse events (AEs) after the second dose ^[16] |
|-----------------|---|

End point description:

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

End point timeframe:

Occurring within Day 0-30 following vaccination

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: The analysis was based only on subjects receiving a second dose of vaccination.

| End point values | Nimenrix Group | Infanrix-Hexa Group | | |
|-----------------------------|-------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 215 | 221 | | |
| Units: Subjects | | | | |
| Any AE(s) | 87 | 79 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any serious adverse events (SAEs)

| | |
|-----------------|--|
| End point title | Number of subjects reporting any serious adverse events (SAEs) |
|-----------------|--|

End point description:

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

End point timeframe:

From dose 1 up to study end

| End point values | Nimenrix + Infanrix-hexa Group | Nimenrix Group | Infanrix-Hexa Group | Meningitec Group |
|-----------------------------|--------------------------------------|-------------------|------------------------|---------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 222 | 220 | 224 | 127 |
| Units: Subjects | | | | |
| Any SAE(s) | 10 | 8 | 11 | 6 |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

SAEs were reported throughout the entire study period. Solicited symptoms were reported during a 4-day period (Day 0-Day 3) after any vaccine dose, while unsolicited AEs were collected within 31 days (Days 0-30) after vaccination.

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

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 11.1 |

Reporting groups

| | |
|--------------------------------|--------------------------------|
| Reporting group title | Nimenrix + Infanrix-hexa Group |
| Reporting group description: - | |
| Reporting group title | Nimenrix Group |
| Reporting group description: - | |
| Reporting group title | Infanrix-Hexa Group |
| Reporting group description: - | |
| Reporting group title | Meningitec Group |
| Reporting group description: - | |

| Serious adverse events | Nimenrix + Infanrix-hexa Group | Nimenrix Group | Infanrix-Hexa Group |
|---|--------------------------------|-----------------|---------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 10 / 222 (4.50%) | 8 / 220 (3.64%) | 11 / 224 (4.91%) |
| number of deaths (all causes) | 0 | 0 | 1 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Concussion | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 1 / 220 (0.45%) | 0 / 224 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Animal bite | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 220 (0.45%) | 0 / 224 (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 |
| Contusion | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 220 (0.00%) | 0 / 224 (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 |

| | | | |
|--|-----------------|-----------------|-----------------|
| Skull fracture | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 220 (0.45%) | 0 / 224 (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 |
| Nervous system disorders | | | |
| Febrile convulsion | | | |
| subjects affected / exposed | 2 / 222 (0.90%) | 0 / 220 (0.00%) | 1 / 224 (0.45%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 220 (0.45%) | 0 / 224 (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 |
| General disorders and administration site conditions | | | |
| Cyst | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 0 / 220 (0.00%) | 1 / 224 (0.45%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Drowning | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 0 / 220 (0.00%) | 1 / 224 (0.45%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 220 (0.00%) | 0 / 224 (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 |
| Immune system disorders | | | |
| Hypersensitivity | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 0 / 220 (0.00%) | 0 / 224 (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 | | | |
| Aphthous stomatitis | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 220 (0.45%) | 0 / 224 (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 | | | |
| Bronchospasm | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 0 / 220 (0.00%) | 1 / 224 (0.45%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 220 (0.45%) | 0 / 224 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 1 / 220 (0.45%) | 2 / 224 (0.89%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis rotavirus | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 1 / 220 (0.45%) | 2 / 224 (0.89%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 220 (0.00%) | 0 / 224 (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 |
| Gastroenteritis norovirus | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 220 (0.00%) | 1 / 224 (0.45%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchopneumonia | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 220 (0.45%) | 1 / 224 (0.45%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Otitis media | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 0 / 220 (0.00%) | 1 / 224 (0.45%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Coxsackie viral infection | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 220 (0.00%) | 0 / 224 (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 |
| Croup infectious | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 0 / 220 (0.00%) | 1 / 224 (0.45%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 0 / 220 (0.00%) | 1 / 224 (0.45%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia respiratory syncytial viral | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 220 (0.00%) | 0 / 224 (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 |
| Subcutaneous abscess | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 1 / 220 (0.45%) | 0 / 224 (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 |
| Tonsillitis | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 220 (0.00%) | 0 / 224 (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 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 222 (0.45%) | 0 / 220 (0.00%) | 0 / 224 (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 |
| Urinary tract infection | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 222 (0.00%) | 0 / 220 (0.00%) | 1 / 224 (0.45%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Iron deficiency | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 0 / 220 (0.00%) | 0 / 224 (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 | Meningitec Group | | |
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 6 / 127 (4.72%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Injury, poisoning and procedural complications | | | |
| Concussion | | | |
| subjects affected / exposed | 0 / 127 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Animal bite | | | |
| subjects affected / exposed | 0 / 127 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Contusion | | | |
| subjects affected / exposed | 0 / 127 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skull fracture | | | |
| subjects affected / exposed | 0 / 127 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Febrile convulsion | | | |

| | | | |
|--|-----------------|--|--|
| subjects affected / exposed | 0 / 127 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 127 (0.79%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Cyst | | | |
| subjects affected / exposed | 0 / 127 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Drowning | | | |
| subjects affected / exposed | 0 / 127 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 127 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Immune system disorders | | | |
| Hypersensitivity | | | |
| subjects affected / exposed | 1 / 127 (0.79%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Aphthous stomatitis | | | |
| subjects affected / exposed | 0 / 127 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Bronchospasm | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 127 (0.79%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 0 / 127 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 127 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastroenteritis rotavirus | | | |
| subjects affected / exposed | 0 / 127 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bronchitis | | | |
| subjects affected / exposed | 2 / 127 (1.57%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastroenteritis norovirus | | | |
| subjects affected / exposed | 1 / 127 (0.79%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bronchopneumonia | | | |
| subjects affected / exposed | 0 / 127 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Otitis media | | | |
| subjects affected / exposed | 1 / 127 (0.79%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Coxsackie viral infection | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 0 / 127 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Croup infectious | | | |
| subjects affected / exposed | 0 / 127 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 127 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia respiratory syncytial viral | | | |
| subjects affected / exposed | 0 / 127 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Subcutaneous abscess | | | |
| subjects affected / exposed | 0 / 127 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 127 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 127 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 127 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Iron deficiency | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 127 (0.79%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Nimenrix + Infanrix-hexa Group | Nimenrix Group | Infanrix-Hexa Group |
|---|--------------------------------|-------------------|---------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 85 / 222 (38.29%) | 87 / 220 (39.55%) | 99 / 224 (44.20%) |
| General disorders and administration site conditions | | | |
| Pain (after meningococcal vaccination) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 49 / 222 (22.07%) | 30 / 220 (13.64%) | 35 / 224 (15.63%) |
| occurrences (all) | 49 | 30 | 35 |
| Redness (after meningococcal vaccination) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 70 / 222 (31.53%) | 74 / 220 (33.64%) | 56 / 224 (25.00%) |
| occurrences (all) | 70 | 74 | 56 |
| Swelling (after meningococcal vaccination) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 42 / 222 (18.92%) | 36 / 220 (16.36%) | 36 / 224 (16.07%) |
| occurrences (all) | 42 | 36 | 36 |
| Pain (after Infanrix-hexa vaccination) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 60 / 222 (27.03%) | 65 / 220 (29.55%) | 64 / 224 (28.57%) |
| occurrences (all) | 60 | 65 | 64 |
| Redness (after infanrix-hexa vaccination) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 70 / 222 (31.53%) | 77 / 220 (35.00%) | 99 / 224 (44.20%) |
| occurrences (all) | 70 | 77 | 99 |
| Swelling (after infanrix-hexa vaccination) | | | |
| alternative assessment type: | | | |

| | | | |
|--|-------------------|-------------------|-------------------|
| Systematic | | | |
| subjects affected / exposed | 48 / 222 (21.62%) | 53 / 220 (24.09%) | 74 / 224 (33.04%) |
| occurrences (all) | 48 | 53 | 74 |
| Drowsiness (after the first dose) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 85 / 222 (38.29%) | 56 / 220 (25.45%) | 80 / 224 (35.71%) |
| occurrences (all) | 85 | 56 | 80 |
| Fever - Rectally (after the first dose) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 80 / 222 (36.04%) | 41 / 220 (18.64%) | 71 / 224 (31.70%) |
| occurrences (all) | 80 | 41 | 71 |
| Irritability (after the first dose) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 83 / 222 (37.39%) | 63 / 220 (28.64%) | 75 / 224 (33.48%) |
| occurrences (all) | 83 | 63 | 75 |
| Loss of appetite (after the first dose) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 51 / 222 (22.97%) | 46 / 220 (20.91%) | 51 / 224 (22.77%) |
| occurrences (all) | 51 | 46 | 51 |
| Drowsiness (after the second dose) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 63 / 220 (28.64%) | 56 / 224 (25.00%) |
| occurrences (all) | 0 | 63 | 56 |
| Fever - Rectally (after the second dose) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 60 / 220 (27.27%) | 37 / 224 (16.52%) |
| occurrences (all) | 0 | 60 | 37 |
| Irritability (after the second dose) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 75 / 220 (34.09%) | 50 / 224 (22.32%) |
| occurrences (all) | 0 | 75 | 50 |
| Loss of appetite (after the second dose) | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|--|----------------------|-------------------------|-------------------------|
| subjects affected / exposed occurrences (all) | 0 / 222 (0.00%) 0 | 54 / 220 (24.55%) 54 | 38 / 224 (16.96%) 38 |
| Infections and infestations | | | |
| Upper respiratory tract infection (after the first dose) | | | |
| subjects affected / exposed | 12 / 222 (5.41%) | 13 / 220 (5.91%) | 12 / 224 (5.36%) |
| occurrences (all) | 12 | 13 | 12 |
| Rhinitis (after the first dose) | | | |
| subjects affected / exposed | 9 / 222 (4.05%) | 11 / 220 (5.00%) | 0 / 224 (0.00%) |
| occurrences (all) | 9 | 11 | 0 |
| Upper respiratory tract infection (after the second dose) | | | |
| subjects affected / exposed | 4 / 222 (1.80%) | 17 / 220 (7.73%) | 14 / 224 (6.25%) |
| occurrences (all) | 4 | 17 | 14 |
| Gastroenteritis (after the second dose) | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 12 / 220 (5.45%) | 8 / 224 (3.57%) |
| occurrences (all) | 0 | 12 | 8 |
| Bronchitis (after the second dose) | | | |
| subjects affected / exposed | 0 / 222 (0.00%) | 11 / 220 (5.00%) | 7 / 224 (3.13%) |
| occurrences (all) | 0 | 11 | 7 |
| Bronchitis (after the first dose) | | | |
| subjects affected / exposed | 7 / 222 (3.15%) | 0 / 220 (0.00%) | 6 / 224 (2.68%) |
| occurrences (all) | 7 | 0 | 6 |

| | | | |
|--|-------------------|--|--|
| Non-serious adverse events | Meningitec Group | | |
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 42 / 127 (33.07%) | | |
| General disorders and administration site conditions | | | |
| Pain (after meningococcal vaccination) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 16 / 127 (12.60%) | | |
| occurrences (all) | 16 | | |
| Redness (after meningococcal vaccination) | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|--|-------------------|--|--|
| subjects affected / exposed | 36 / 127 (28.35%) | | |
| occurrences (all) | 36 | | |
| Swelling (after meningococcal vaccination) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 23 / 127 (18.11%) | | |
| occurrences (all) | 23 | | |
| Pain (after Infanrix-hexa vaccination) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 127 (0.00%) | | |
| occurrences (all) | 0 | | |
| Redness (after infanrix-hexa vaccination) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 127 (0.00%) | | |
| occurrences (all) | 0 | | |
| Swelling (after infanrix-hexa vaccination) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 127 (0.00%) | | |
| occurrences (all) | 0 | | |
| Drowsiness (after the first dose) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 29 / 127 (22.83%) | | |
| occurrences (all) | 29 | | |
| Fever - Rectally (after the first dose) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 15 / 127 (11.81%) | | |
| occurrences (all) | 15 | | |
| Irritability (after the first dose) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 25 / 127 (19.69%) | | |
| occurrences (all) | 25 | | |
| Loss of appetite (after the first dose) | | | |
| alternative assessment type: Systematic | | | |

| | | | |
|--|-------------------|--|--|
| subjects affected / exposed | 15 / 127 (11.81%) | | |
| occurrences (all) | 15 | | |
| Drowsiness (after the second dose) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 127 (0.00%) | | |
| occurrences (all) | 0 | | |
| Fever - Rectally (after the second dose) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 127 (0.00%) | | |
| occurrences (all) | 0 | | |
| Irritability (after the second dose) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 127 (0.00%) | | |
| occurrences (all) | 0 | | |
| Loss of appetite (after the second dose) | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 127 (0.00%) | | |
| occurrences (all) | 0 | | |
| Infections and infestations | | | |
| Upper respiratory tract infection (after the first dose) | | | |
| subjects affected / exposed | 8 / 127 (6.30%) | | |
| occurrences (all) | 8 | | |
| Rhinitis (after the first dose) | | | |
| subjects affected / exposed | 0 / 127 (0.00%) | | |
| occurrences (all) | 0 | | |
| Upper respiratory tract infection (after the second dose) | | | |
| subjects affected / exposed | 0 / 127 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastroenteritis (after the second dose) | | | |
| subjects affected / exposed | 0 / 127 (0.00%) | | |
| occurrences (all) | 0 | | |
| Bronchitis (after the second dose) | | | |

| | | | |
|-----------------------------------|-----------------|--|--|
| subjects affected / exposed | 0 / 127 (0.00%) | | |
| occurrences (all) | 0 | | |
| Bronchitis (after the first dose) | | | |
| subjects affected / exposed | 7 / 127 (5.51%) | | |
| occurrences (all) | 7 | | |

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