



Clinical trial results:

A phase IIIb, open, multi-country, controlled, randomized study to demonstrate the immunogenicity and safety of GSK Biologicals' meningococcal conjugate vaccine, MenACWY-TT (GSK 134612) in healthy infants, given on a 3+1 primary and booster (2, 4, 6 and 15-18 months of age), a 1+1 primary and booster (6 and 15-18 months of age) or as a single dose at 15-18 months of age.

Summary

| | |
|--------------------------|-----------------|
| EudraCT number | 2013-002537-37 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 19 October 2015 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v2 (current) |
| This version publication date | 26 May 2022 |
| First version publication date | 29 April 2016 |
| Version creation reason | |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | 114858 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01340898 |
| 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, +44 2089904466, GSKClinicalSupportHD@gsk.com |
| Scientific contact | Clinical Trials Call Center, GlaxoSmithKline Biologicals, +44 2089904466, 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? | No |

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 18 November 2016 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 19 October 2015 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the immunogenicity of the MenACWY-TT conjugate vaccine in terms of bactericidal antibodies to *N. meningitidis* serogroups A, C, W-135 and Y one month post-dose 3 of MenACWY-TT at 7 months of age in healthy infants. Criteria for immunogenicity: For each serogroup, one month after dose 3 of MenACWY-TT vaccination, the lower limit of the two-sided exact 95% confidence interval (CI) for the percentage of subjects with rSBA titre $\geq 1:8$ is greater than or equal to the pre-defined clinical limit of 80%.

Protection of trial subjects:

All subjects were supervised closely for at least 30 minutes following vaccination with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines. Subjects were followed-up from the time the subject consents to participate in the study until she/he is discharged.

Background therapy: -

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 27 January 2012 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Efficacy |
| Long term follow-up duration | 6 Months |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------|
| Country: Number of subjects enrolled | Mexico: 351 |
| Country: Number of subjects enrolled | Lebanon: 402 |
| Worldwide total number of subjects | 753 |
| EEA total number of subjects | 0 |

Notes:

Subjects enrolled per age group

| | |
|---|-----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 | 753 |

| | |
|---------------------------|---|
| months) | |
| 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:

Out of 753 subjects enrolled, 3 subjects were not vaccinated and hence not considered to have started the study.

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.

Pre-assignment period milestones

| | |
|------------------------------|-----|
| Number of subjects started | 753 |
| Number of subjects completed | 750 |

Pre-assignment subject non-completion reasons

| | |
|----------------------------|-------------------|
| Reason: Number of subjects | No vaccination: 3 |
|----------------------------|-------------------|

Period 1

| | |
|------------------------------|-------------------------|
| Period 1 title | Primary Phase |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

| | |
|------------------------------|--------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | Nimenrix 3+1 Group |

Arm description:

Subjects, male and female, received 4 doses of Nimenrix vaccine (3 doses at 2, 4 and 6 months of age followed by a booster dose at 15-18 months of age) and 4 doses of Synflorix and Infanrix-IPV/Hiberix vaccines (at 2, 4, 6 and 15-18 months of age). All vaccines were administered intramuscularly (IM) in the anterolateral region of the thigh.

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Nimenrix |
| Investigational medicinal product code | |
| Other name | MenACWY-TT vaccine, GSK134612 |
| Pharmaceutical forms | Powder and solvent for solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

The 3 vaccine doses were administered in the anterolateral region of the thigh at 2, 4 and 6 months of age.

| | |
|--|--------------------------|
| Investigational medicinal product name | Synflorix |
| Investigational medicinal product code | |
| Other name | 10Pn vaccine |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

As part of the study all subjects received routine administration of Synflorix at 2, 4 and 6 months of age, administered intramuscularly (IM) in the anterolateral region of the thigh.

| | |
|--|--------------|
| Investigational medicinal product name | Infanrix-IPV |
| Investigational medicinal product code | |
| Other name | |

| | |
|--|---|
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details: | |
| As part of the study all subjects received routine administration of Infanrix-IPV vaccine at 2, 4 and 6 months of age, administered intramuscularly (IM) in the anterolateral region of the thigh. | |
| Investigational medicinal product name | Hiberix |
| Investigational medicinal product code | |
| Other name | Hib vaccine |
| Pharmaceutical forms | Powder and solvent for solution for injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details: | |
| As part of the study all subjects received routine administration of Hib vaccine at 2, 4 and 6 months of age, administered intramuscularly (IM) in the anterolateral region of the thigh. | |
| Arm title | Nimenrix 1+1 Group |
| Arm description: | |
| Subjects, male and female, received 2 doses of Nimenrix vaccine (1 dose at 6 months of age followed by a booster dose at 15-18 months of age) and 4 doses of Synflorix and Infanrix-IPV/Hiberix vaccines (at 2, 4, 6 and 15-18 months of age). All vaccines were administered intramuscularly (IM) in the anterolateral region of the thigh. | |
| Arm type | Experimental |
| Investigational medicinal product name | Synflorix |
| Investigational medicinal product code | |
| Other name | 10Ph vaccine |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details: | |
| As part of the study all subjects received routine administration of Synflorix at 2, 4 and 6 months of age, administered intramuscularly (IM) in the anterolateral region of the thigh. | |
| Investigational medicinal product name | Infanrix-IPV |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details: | |
| As part of the study all subjects received routine administration of Infanrix-IPV vaccine at 2, 4 and 6 months of age, administered intramuscularly (IM) in the anterolateral region of the thigh. | |
| Investigational medicinal product name | Hiberix |
| Investigational medicinal product code | |
| Other name | Hib vaccine |
| Pharmaceutical forms | Powder and solvent for solution for injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details: | |
| As part of the study all subjects received routine administration of Hib vaccine at 2, 4 and 6 months of age, administered intramuscularly (IM) in the anterolateral region of the thigh. | |
| Investigational medicinal product name | Nimenrix |
| Investigational medicinal product code | |
| Other name | MenACWY-TT vaccine, GSK134612 |
| Pharmaceutical forms | Powder and solvent for solution for injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details: | |
| The vaccine was administered in the anterolateral region of the thigh at 6 months of age. | |
| Arm title | Nimenrix Control Group |
| Arm description: | |
| Subjects, male and female, received 1 dose of Nimenrix at 15-18 months of age and 4 doses of | |

Synflorix and Infanrix-IPV/Hiberix vaccines (at 2, 4, 6 and 15-18 months of age). All vaccines were administered intramuscularly (IM) in the anterolateral region of the thigh.

| | |
|--|--------------------------|
| Arm type | Active comparator |
| Investigational medicinal product name | Synflorix |
| Investigational medicinal product code | |
| Other name | 10Pn vaccine |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

As part of the study all subjects received routine administration of Synflorix at 2, 4 and 6 months of age, administered intramuscularly (IM) in the anterolateral region of the thigh.

| | |
|--|--------------------------|
| Investigational medicinal product name | Infanrix-IPV |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

As part of the study all subjects received routine administration of Infanrix-IPV vaccine at 2, 4 and 6 months of age, administered intramuscularly (IM) in the anterolateral region of the thigh.

| | |
|--|---|
| Investigational medicinal product name | Hiberix |
| Investigational medicinal product code | |
| Other name | Hib vaccine |
| Pharmaceutical forms | Powder and solvent for solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

As part of the study all subjects received routine administration of Hib vaccine at 2, 4 and 6 months of age, administered intramuscularly (IM) in the anterolateral region of the thigh.

| Number of subjects in period 1^[1] | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix Control Group |
|---|--------------------|--------------------|------------------------|
| Started | 376 | 187 | 187 |
| Completed | 360 | 178 | 181 |
| Not completed | 16 | 9 | 6 |
| Consent withdrawn by subject | 8 | 7 | 5 |
| Migrated/moved from study area | 4 | 1 | - |
| Lost to follow-up | 4 | 1 | - |
| Serious Adverse Events | - | - | 1 |

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Not all subjects who completed a period entered in the next one. The number of subjects who started each period depends on the number of subjects available at the time.

Period 2

| | |
|------------------------------|-------------------------|
| Period 2 title | Booster Phase |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

Arms

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

| | |
|------------------|--------------------|
| Arm title | Nimenrix 3+1 Group |
|------------------|--------------------|

Arm description:

Subjects who received booster 1 dose of Nimenrix vaccine at 15-18 months of age.

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Nimenrix |
| Investigational medicinal product code | |
| Other name | MenACWY-TT vaccine, GSK134612 |
| Pharmaceutical forms | Powder and solvent for solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

The vaccine was administered in the anterolateral region of the thigh at 15-18 months of age.

| | |
|--|--------------------------|
| Investigational medicinal product name | Synflorix |
| Investigational medicinal product code | |
| Other name | 10Pn vaccine |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

As part of the study all subjects received routine administration of Synflorix at 15-18 months of age, administered intramuscularly (IM) in the anterolateral region of the thigh.

| | |
|--|--------------------------|
| Investigational medicinal product name | Infanrix-IPV |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

As part of the study all subjects received routine administration of Infanrix-IPV vaccine at 15-18 months of age, administered intramuscularly (IM) in the anterolateral region of the thigh.

| | |
|--|---|
| Investigational medicinal product name | Hiberix |
| Investigational medicinal product code | |
| Other name | Hib vaccine |
| Pharmaceutical forms | Powder and solvent for solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

As part of the study all subjects received routine administration of Hib vaccine at 15-18 months of age, administered intramuscularly (IM) in the anterolateral region of the thigh.

| | |
|------------------|--------------------|
| Arm title | Nimenrix 1+1 Group |
|------------------|--------------------|

Arm description:

Subjects who received booster 1 dose of Nimenrix vaccine 15-18 months of age.

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Nimenrix |
| Investigational medicinal product code | |
| Other name | MenACWY-TT vaccine, GSK134612 |
| Pharmaceutical forms | Powder and solvent for solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

The vaccine was administered in the anterolateral region of the thigh at 15-18 months of age.

| | |
|--|--------------------------|
| Investigational medicinal product name | Synflorix |
| Investigational medicinal product code | |
| Other name | 10Pn vaccine |
| Pharmaceutical forms | Suspension for injection |

| | |
|---|---|
| Routes of administration | Intramuscular use |
| Dosage and administration details: | |
| As part of the study all subjects received routine administration of Synflorix at 15-18 months of age, administered intramuscularly (IM) in the anterolateral region of the thigh. | |
| Investigational medicinal product name | Infanrix-IPV |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |
| Dosage and administration details: | |
| As part of the study all subjects received routine administration of Infanrix-IPV vaccine at 15-18 months of age, administered intramuscularly (IM) in the anterolateral region of the thigh. | |
| Investigational medicinal product name | Hiberix |
| Investigational medicinal product code | |
| Other name | Hib vaccine |
| Pharmaceutical forms | Powder and solvent for solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

As part of the study all subjects received routine administration of Hib vaccine at 15-18 months of age, administered intramuscularly (IM) in the anterolateral region of the thigh.

| | |
|------------------|------------------|
| Arm title | Nimenrix 1 Group |
|------------------|------------------|

Arm description:

Subjects who received 1 dose of Nimenrix vaccine at 15-18 months of age.

| | |
|--|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Nimenrix |
| Investigational medicinal product code | |
| Other name | MenACWY-TT vaccine, GSK134612 |
| Pharmaceutical forms | Powder and solvent for solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

The vaccine was administered in the anterolateral region of the thigh at 15-18 months of age.

| | |
|--|--------------------------|
| Investigational medicinal product name | Synflorix |
| Investigational medicinal product code | |
| Other name | 10Pn vaccine |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

As part of the study all subjects received routine administration of Synflorix at 15-18 months of age, administered intramuscularly (IM) in the anterolateral region of the thigh.

| | |
|--|---|
| Investigational medicinal product name | Hiberix |
| Investigational medicinal product code | |
| Other name | Hib vaccine |
| Pharmaceutical forms | Powder and solvent for solution for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

As part of the study all subjects received routine administration of Hib vaccine at 15-18 months of age, administered intramuscularly (IM) in the anterolateral region of the thigh.

| Number of subjects in period 2^[2] | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix 1 Group |
|---|--------------------|--------------------|------------------|
| Started | 342 | 166 | 170 |
| Completed | 332 | 164 | 163 |
| Not completed | 10 | 2 | 7 |
| Consent withdrawn by subject | 3 | - | 4 |
| Migrated/moved from study area | 3 | - | - |
| Lost to follow-up | 4 | 2 | 3 |

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Not all subjects who completed a period entered in the next one. The number of subjects who started each period depends on the number of subjects available at the time.

Baseline characteristics

Reporting groups

| | |
|-----------------------|--------------------|
| Reporting group title | Nimenrix 3+1 Group |
|-----------------------|--------------------|

Reporting group description:

Subjects, male and female, received 4 doses of Nimenrix vaccine (3 doses at 2, 4 and 6 months of age followed by a booster dose at 15-18 months of age) and 4 doses of Synflorix and Infanrix-IPV/Hiberix vaccines (at 2, 4, 6 and 15-18 months of age). All vaccines were administered intramuscularly (IM) in the anterolateral region of the thigh.

| | |
|-----------------------|--------------------|
| Reporting group title | Nimenrix 1+1 Group |
|-----------------------|--------------------|

Reporting group description:

Subjects, male and female, received 2 doses of Nimenrix vaccine (1 dose at 6 months of age followed by a booster dose at 15-18 months of age) and 4 doses of Synflorix and Infanrix-IPV/Hiberix vaccines (at 2, 4, 6 and 15-18 months of age). All vaccines were administered intramuscularly (IM) in the anterolateral region of the thigh.

| | |
|-----------------------|------------------------|
| Reporting group title | Nimenrix Control Group |
|-----------------------|------------------------|

Reporting group description:

Subjects, male and female, received 1 dose of Nimenrix at 15-18 months of age and 4 doses of Synflorix and Infanrix-IPV/Hiberix vaccines (at 2, 4, 6 and 15-18 months of age). All vaccines were administered intramuscularly (IM) in the anterolateral region of the thigh.

| Reporting group values | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix Control Group |
|------------------------|--------------------|--------------------|------------------------|
| Number of subjects | 376 | 187 | 187 |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|---|-------|-------|-------|
| Age continuous | | | |
| Units: weeks | | | |
| arithmetic mean | 8.1 | 8.1 | 8.2 |
| standard deviation | ± 1.6 | ± 1.7 | ± 1.7 |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 182 | 105 | 95 |
| Male | 194 | 82 | 92 |
| Race/Ethnicity, Customized | | | |
| Units: Subjects | | | |
| White - Arabic / North African Heritage | 199 | 100 | 99 |
| White - Caucasian / European Heritage | 1 | 0 | 1 |
| Mixed Origin | 176 | 87 | 87 |

| Reporting group values | Total | | |
|------------------------|-------|--|--|
| Number of subjects | 750 | | |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|--------------------|---|--|--|
| Age continuous | | | |
| Units: weeks | | | |
| arithmetic mean | | | |
| standard deviation | - | | |

| | | | |
|---|-----|--|--|
| Gender categorical Units: Subjects | | | |
| Female | 382 | | |
| Male | 368 | | |
| Race/Ethnicity, Customized Units: Subjects | | | |
| White - Arabic / North African Heritage | 398 | | |
| White - Caucasian / European Heritage | 2 | | |
| Mixed Origin | 350 | | |

End points

End points reporting groups

| | |
|--|------------------------|
| Reporting group title | Nimenrix 3+1 Group |
| Reporting group description: Subjects, male and female, received 4 doses of Nimenrix vaccine (3 doses at 2, 4 and 6 months of age followed by a booster dose at 15-18 months of age) and 4 doses of Synflorix and Infanrix-IPV/Hiberix vaccines (at 2, 4, 6 and 15-18 months of age). All vaccines were administered intramuscularly (IM) in the anterolateral region of the thigh. | |
| Reporting group title | Nimenrix 1+1 Group |
| Reporting group description: Subjects, male and female, received 2 doses of Nimenrix vaccine (1 dose at 6 months of age followed by a booster dose at 15-18 months of age) and 4 doses of Synflorix and Infanrix-IPV/Hiberix vaccines (at 2, 4, 6 and 15-18 months of age). All vaccines were administered intramuscularly (IM) in the anterolateral region of the thigh. | |
| Reporting group title | Nimenrix Control Group |
| Reporting group description: Subjects, male and female, received 1 dose of Nimenrix at 15-18 months of age and 4 doses of Synflorix and Infanrix-IPV/Hiberix vaccines (at 2, 4, 6 and 15-18 months of age). All vaccines were administered intramuscularly (IM) in the anterolateral region of the thigh. | |
| Reporting group title | Nimenrix 3+1 Group |
| Reporting group description: Subjects who received booster 1 dose of Nimenrix vaccine at 15-18 months of age. | |
| Reporting group title | Nimenrix 1+1 Group |
| Reporting group description: Subjects who received booster 1 dose of Nimenrix vaccine 15-18 months of age. | |
| Reporting group title | Nimenrix 1 Group |
| Reporting group description: Subjects who received 1 dose of Nimenrix vaccine at 15-18 months of age. | |

Primary: Number of subjects with serum bactericidal assay using rabbit complement against *Neisseria meningitidis* serogroups antibody titers greater than or equal to (\geq) the cut-off value for the Nimenrix 3+1 Group

| | |
|--|--|
| End point title | Number of subjects with serum bactericidal assay using rabbit complement against <i>Neisseria meningitidis</i> serogroups antibody titers greater than or equal to (\geq) the cut-off value for the Nimenrix 3+1 Group ^{[1][2]} |
| End point description: The cut-off value for the rSBA titers was $\geq 1:8$. <i>Neisseria meningitidis</i> serogroups A, C, W-135, Y (rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY) antibodies were assessed. Immunogenicity was considered demonstrated if the lower limit of the two-sided exact 95% confidence interval (CI) for the percentage of subjects with rSBA titre $\geq 1:8$ was greater than or equal to the pre-defined clinical limit of 80%. | |
| End point type | Primary |
| End point timeframe: At Month 5 (one month post dose 3) | |

Notes:

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

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

[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: Not all arms in the Baseline Period are applicable for this endpoint.

| | | | | |
|-----------------------------|--------------------|--|--|--|
| End point values | Nimenrix 3+1 Group | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 328 | | | |
| Units: Participants | | | | |
| rSBA-MenA [N=328] | 328 | | | |
| rSBA-MenC [N=328] | 327 | | | |
| rSBA-MenW-135 [N=327] | 325 | | | |
| rSBA-MenY [N=328] | 327 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY antibody titers greater than or equal to (\geq) the 1:8 for the Nimenrix 3+1 Group

| | |
|-----------------|---|
| End point title | Number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY antibody titers greater than or equal to (\geq) the 1:8 for the Nimenrix 3+1 Group ^[3] |
|-----------------|---|

End point description:

The cut-off value for the rSBA titers was \geq 1:8

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

End point timeframe:

At Month 13 (prior to booster dose) and at Month 14 (one month after booster dose)

Notes:

[3] - 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: Not all arms in the Baseline Period are applicable for this endpoint.

| | | | | |
|-----------------------------|--------------------|--|--|--|
| End point values | Nimenrix 3+1 Group | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 284 | | | |
| Units: Participants | | | | |
| rSBA-MenA,M13 [N=276] | 225 | | | |
| rSBA-MenA,M14 [N=283] | 283 | | | |
| rSBA-MenC,M13 [N=276] | 190 | | | |
| rSBA-MenC,M14 [N=283] | 282 | | | |
| rSBA-MenW-135,M13 [N=257] | 225 | | | |
| rSBA-MenW-135,M14 [N=284] | 284 | | | |
| rSBA-MenY,M13 [N=275] | 240 | | | |
| rSBA-MenY,M14[N=284] | 284 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and

rSBA-MenY antibody titers greater than or equal to (\geq) the 1:128 for the Nimenrix 3+1 Group

| | |
|-----------------|---|
| End point title | Number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY antibody titers greater than or equal to (\geq) the 1:128 for the Nimenrix 3+1 Group ^[4] |
|-----------------|---|

End point description:

The cut-off value for the rSBA titers was \geq 1:128

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

End point timeframe:

At Month 5 (one month post dose 3), 13 (prior booster dose) and 14 (one month after booster dose)

Notes:

[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: Not all arms in the Baseline Period are applicable for this endpoint.

| End point values | Nimenrix 3+1 Group | | | |
|-----------------------------|--------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 328 | | | |
| Units: Participants | | | | |
| rSBA-MenA, M5 [N=328] | 321 | | | |
| rSBA-MenA, M13 [N=276] | 146 | | | |
| rSBA-MenA, M14 [N=283] | 282 | | | |
| rSBA-MenC, M5 [N=328] | 318 | | | |
| rSBA-MenC, M13 [N=276] | 93 | | | |
| rSBA-MenC, M14 [N=283] | 282 | | | |
| rSBA-MenW-135, M5 [N=327] | 313 | | | |
| rSBA-MenW-135, M13 [N=275] | 122 | | | |
| rSBA-MenW-135, M14 [N=284] | 284 | | | |
| rSBA-MenY, M5 [N=328] | 312 | | | |
| rSBA-MenY, M13 [N=275] | 121 | | | |
| rSBA-MenY, M14 [N=284] | 283 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY antibody titers for the Nimenrix 3+1 Group

| | |
|-----------------|---|
| End point title | rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY antibody titers for the Nimenrix 3+1 Group ^[5] |
|-----------------|---|

End point description:

Antibody titers are presented as geometric mean titers (GMTs).

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

End point timeframe:

At Month 5 (one month post dose 3), 13 (prior booster dose) and 14 (one month after booster dose)

Notes:

[5] - 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: Not all arms in the Baseline Period are applicable for this endpoint.

| | | | | |
|--|---------------------------|--|--|--|
| End point values | Nimenrix 3+1 Group | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 328 | | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| rSBA-MenA, M5 [N=328] | 577.5 (520.7 to 640.6) | | | |
| rSBA-MenA, M13 [N=276] | 71.1 (56.6 to 89.3) | | | |
| rSBA-MenA, M14 [N=283] | 2366.4 (2134.8 to 2623.1) | | | |
| rSBA-MenC, M5 [N=328] | 803.1 (710.4 to 907.8) | | | |
| rSBA-MenC, M13 [N=276] | 33.9 (27.4 to 41.9) | | | |
| rSBA-MenC, M14 [N=283] | 2761.2 (2461.2 to 3097.9) | | | |
| rSBA-MenW-135, M5 [N=327] | 1190.3 (1019.3 to 1390.1) | | | |
| rSBA-MenW-135, M13 [N=275] | 52.0 (42.2 to 64.2) | | | |
| rSBA-MenW-135, M14 [N=284] | 3696.9 (3242.8 to 4214.7) | | | |
| rSBA-MenY, M5 [N=328] | 647.4 (566.6 to 739.6) | | | |
| rSBA-MenY, M13 [N=275] | 66.3 (54.3 to 81.0) | | | |
| rSBA-MenY, M14 [N=284] | 2778.6 (2472.5 to 3122.5) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY antibody titers greater than or equal to (\geq) the cut-off values for the Nimenrix 1+1 and Nimenrix Control Groups

| | |
|-----------------|--|
| End point title | Number of subjects with rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY antibody titers greater than or equal to (\geq) the cut-off values for the Nimenrix 1+1 and Nimenrix Control Groups ^[6] |
|-----------------|--|

End point description:

The cut-off values for the rSBA antibody titers were $\geq 1:8$ and $\geq 1:128$

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

End point timeframe:

At Months 5 (one month post-primary dose for Nimenrix 1+1 Group), 13 (prior booster dose for Nimenrix 1+1 and prior primary dose for Nimenrix Control Group) and 14 (post booster dose for Nimenrix 1+1 and post-primary dose for Nimenrix Control Group)

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: Not all arms in the Baseline Period are applicable for this endpoint.

| End point values | Nimenrix 1+1 Group | Nimenrix Control Group | | |
|--|--------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 163 | 163 | | |
| Units: Participants | | | | |
| rSBA-MenA, M5, $\geq 1:8$ [N=163;163] | 161 | 6 | | |
| rSBA-MenA, M13, $\geq 1:8$ [N=131;132] | 107 | 19 | | |
| rSBA-MenA, M14, $\geq 1:8$ [N=139;135] | 138 | 133 | | |
| rSBA-MenC, M5, $\geq 1:8$ [N=163;162] | 162 | 6 | | |
| rSBA-MenC, M13, $\geq 1:8$ [N=131;132] | 86 | 3 | | |
| rSBA-MenC, M14, $\geq 1:8$ [N=139;135] | 138 | 130 | | |
| rSBA-MenW-135, M5, $\geq 1:8$ [N=163;163] | 153 | 4 | | |
| rSBA-MenW-135, M13, $\geq 1:8$ [N=131;132] | 102 | 7 | | |
| rSBA-MenW-135, M14, $\geq 1:8$ [N=139;135] | 139 | 131 | | |
| rSBA-MenY, M5, $\geq 1:8$ [N=163;162] | 161 | 16 | | |
| rSBA-MenY, M13, $\geq 1:8$ [N=131;132] | 116 | 24 | | |
| rSBA-MenY, M14, $\geq 1:8$ [N=139;135] | 139 | 131 | | |
| rSBA-MenA, M5, $\geq 1:128$ [N=163;163] | 155 | 6 | | |
| rSBA-MenA, M13, $\geq 1:128$ [N=131;132] | 88 | 16 | | |
| rSBA-MenA, M14, $\geq 1:128$ [N=139;135] | 138 | 132 | | |
| rSBA-MenC, M5, $\geq 1:128$ [N=163;162] | 151 | 5 | | |
| rSBA-MenC, M13, $\geq 1:128$ [N=131;132] | 39 | 1 | | |
| rSBA-MenC, M14, $\geq 1:128$ [N=139;135] | 137 | 128 | | |
| rSBA-MenW-135, M5, $\geq 1:128$ [N=163;163] | 151 | 4 | | |
| rSBA-MenW-135, M13, $\geq 1:128$ [N=131;132] | 65 | 7 | | |
| rSBA-MenW-135, M14, $\geq 1:128$ [N=139;135] | 138 | 131 | | |
| rSBA-MenY, M5, $\geq 1:128$ [N=163;162] | 159 | 16 | | |
| rSBA-MenY, M13, $\geq 1:128$ [N=131;132] | 70 | 23 | | |
| rSBA-MenY, M14, $\geq 1:128$ [N=139;135] | 137 | 131 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY antibody titers Nimenrix 1+1 and Nimenrix Control Groups

| | |
|--|---|
| End point title | rSBA-MenA, rSBA-MenC, rSBA-MenW-135 and rSBA-MenY antibody titers Nimenrix 1+1 and Nimenrix Control Groups ^[7] |
| End point description: | |
| Antibody titers are presented as geometric mean titers (GMTs). | |
| End point type | Secondary |

End point timeframe:

At Months 5 (one month post-primary dose for Nimenrix 1+1 Group), 13 (prior booster dose for Nimenrix 1+1 and prior primary dose for Nimenrix Control Group) and 14 (post booster dose Nimenrix 1+1 and post-primary dose for Nimenrix Control Group)

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: Not all arms in the Baseline Period are applicable for this endpoint.

| End point values | Nimenrix 1+1 Group | Nimenrix Control Group | | |
|--|---------------------------|---------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 163 | 163 | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| rSBA-MenA, M5, $\geq 1:8$ [N=163;163] | 1332.9 (1035.2 to 1716.2) | 4.8 (4.1 to 5.5) | | |
| rSBA-MenA, M13, $\geq 1:8$ [N=131;132] | 125.3 (84.4 to 186.1) | 7.2 (5.5 to 9.3) | | |
| rSBA-MenA, M14, $\geq 1:8$ [N=139;135] | 2762.3 (2310.3 to 3302.8) | 2918.7 (2264.6 to 3761.7) | | |
| rSBA-MenC, M5, $\geq 1:8$ [N=163;162] | 591.6 (482.3 to 725.8) | 4.7 (4.1 to 5.4) | | |
| rSBA-MenC, M13, $\geq 1:8$ [N=131;132] | 27.4 (20.6 to 36.6) | 4.2 (3.9 to 4.4) | | |
| rSBA-MenC, M14, $\geq 1:8$ [N=139;135] | 2525.2 (2102.1 to 3033.3) | 768.1 (593.0 to 995.0) | | |
| rSBA-MenW-135, M5, $\geq 1:8$ [N=163;163] | 1255.9 (917.0 to 1720.0) | 4.6 (4.0 to 5.2) | | |
| rSBA-MenW-135, M13, $\geq 1:8$ [N=131;132] | 63.3 (45.6 to 87.9) | 5.0 (4.2 to 5.8) | | |
| rSBA-MenW-135, M14, $\geq 1:8$ [N=139;135] | 3144.7 (2636.9 to 3750.4) | 5240.7 (3855.5 to 7123.7) | | |
| rSBA-MenY, M5, $\geq 1:8$ [N=163;162] | 1469.9 (1186.5 to 1821.0) | 6.3 (5.0 to 7.8) | | |
| rSBA-MenY, M13, $\geq 1:8$ [N=131;132] | 106.4 (76.4 to 148.1) | 9.4 (6.8 to 12.9) | | |
| rSBA-MenY, M14, $\geq 1:8$ [N=139;135] | 2748.6 (2301.4 to 3282.6) | 4202.5 (3219.9 to 5485.1) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with booster responses for rSBA-MenA, C rSBA-MenC, Y rSBA-MenY and W-135 rSBA-MenW-135 in Nimenrix 3+1 and Nimenrix 1+1 Groups and With Vaccine Response in Nimenrix Control Group

| | |
|-----------------|---|
| End point title | Number of subjects with booster responses for rSBA-MenA, C rSBA-MenC, Y rSBA-MenY and W-135 rSBA-MenW-135 in Nimenrix 3+1 and Nimenrix 1+1 Groups and With Vaccine Response in Nimenrix Control Group |
|-----------------|---|

End point description:

Booster response defined as: for seronegative subjects, antibody titre $\geq 1:32$ at post-booster vaccination; for seropositive subjects, antibody titre at post-booster vaccination ≥ 4 -fold the pre-booster vaccination antibody titre; for initially seropositive subjects: antibody titre at M14 ≥ 4 fold the pre-vaccination antibody titre.

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

End point timeframe:

At Month 14 (one month post-booster dose for Nimenrix 3+1 and Nimenrix 1+1 and post-primary dose for Nimenrix Control Group)

| End point values | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix 1 Group | |
|-----------------------------|--------------------|--------------------|------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 275 | 131 | 132 | |
| Units: Participants | | | | |
| rSBA-MenA | 248 | 108 | 125 | |
| rSBA-MenC | 210 | 129 | 126 | |
| rSBA-MenW-135 | 272 | 122 | 128 | |
| rSBA-MenY | 267 | 121 | 125 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serum bactericidal assay using human complement against Neisseria meningitidis serogroups A, C, W-135, Y antibody titers greater than or equal to (\geq) the cut-off value

| | |
|-----------------|---|
| End point title | Number of subjects with serum bactericidal assay using human complement against Neisseria meningitidis serogroups A, C, W-135, Y antibody titers greater than or equal to (\geq) the cut-off value ^[8] |
|-----------------|---|

End point description:

The cut-off value for the hSBA titers was $\geq 1:4$ and $\geq 1:8$.

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

End point timeframe:

At Month 5 (One Month Post-primary for Nimenrix 3+1 and 1+1 Groups)

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: Not all arms in the Baseline Period are applicable for this endpoint.

| End point values | Nimenrix 3+1 Group | Nimenrix 1+1 Group | | |
|--------------------------------------|--------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 147 | 66 | | |
| Units: Participants | | | | |
| hSBA-MenA, $\geq 1:4$ [N=136;59] | 136 | 58 | | |
| hSBA-MenC, $\geq 1:4$ [N=147;66] | 147 | 66 | | |
| hSBA-MenW-135, $\geq 1:4$ [N=107;47] | 107 | 41 | | |
| hSBA-MenY, $\geq 1:4$ [N=127;52] | 127 | 48 | | |

| | | | | |
|--------------------------------------|-----|----|--|--|
| hSBA-MenA, $\geq 1:8$ [N=136;59] | 136 | 58 | | |
| hSBA-MenC, $\geq 1:8$ [N=147;66] | 147 | 66 | | |
| hSBA-MenW-135, $\geq 1:8$ [N=107;47] | 107 | 41 | | |
| hSBA-MenY, $\geq 1:8$ [N=127;52] | 127 | 48 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-Men-Y antibody titers at month 5 (One Month Post-primary for Nimenrix3+1 and Nimenrix 1+1 Groups) -Randomized Subset of 50% of Subjects of All Three Groups

| | |
|-----------------|--|
| End point title | hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-Men-Y antibody titers at month 5 (One Month Post-primary for Nimenrix3+1 and Nimenrix 1+1 Groups) -Randomized Subset of 50% of Subjects of All Three Groups ^[9] |
|-----------------|--|

End point description:

Antibody titers are presented as geometric mean titers (GMTs).

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

End point timeframe:

At Month 5 (one month post-primary for Nimenrix 3+1 and Nimenrix 1+1 Groups)

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: Not all arms in the Baseline Period are applicable for this endpoint.

| End point values | Nimenrix 3+1 Group | Nimenrix 1+1 Group | | |
|--|---------------------------|------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 147 | 66 | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| hSBA-MenA [N=136;59] | 808.0 (683.8 to 954.6) | 270.5 (205.9 to 355.4) | | |
| hSBA-MenC [N=147;66] | 3970.8 (3144.0 to 5015.1) | 523.1 (381.5 to 717.3) | | |
| hSBA-MenW-135 [N=107;47] | 1514.5 (1277.2 to 1795.8) | 136.5 (78.4 to 237.6) | | |
| hSBA-MenY [N=127;52] | 1276.2 (1077.3 to 1511.8) | 194.8 (117.6 to 322.9) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-Men-Y titers greater than or equal to (\geq) the cut-off value (Pre- and Post-

booster for Nimenrix 3+1 and 1+1 Groups and Pre- and Post-vaccination for Nimenrix Control)

| | |
|-----------------|---|
| End point title | Number of subjects with hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-Men-Y titers greater than or equal to (\geq) the cut-off value (Pre- and Post-booster for Nimenrix 3+1 and 1+1 Groups and Pre- and Post-vaccination for Nimenrix Control) ^[10] |
|-----------------|---|

End point description:

The cut-off value for the hSBA titers was $\geq 1:4$ and $\geq 1:8$.

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

End point timeframe:

At Month 13 (pre-booster for Nimenrix 3+1 and Nimenrix 1+1 Groups and pre-vaccination for Nimenrix Control), and at Month 14 (post-booster for Nimenrix 3+1 and Nimenrix 1+1 Groups and post-vaccination for Nimenrix Control)

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: Not all arms in the Baseline Period are applicable for this endpoint.

| End point values | Nimenrix 3+1 Group | Nimenrix 1+1 Group | | |
|--|--------------------|--------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 198 | 92 | | |
| Units: Participants | | | | |
| hSBA-MenA, $\geq 1:4$, M13 [N=152;71] | 131 | 48 | | |
| hSBA-MenA, $\geq 1:4$, M14 [N=173;83] | 173 | 83 | | |
| hSBA-MenC, $\geq 1:4$, M13 [N=173;78] | 168 | 76 | | |
| hSBA-MenC, $\geq 1:4$, M14 [N=198;92] | 198 | 92 | | |
| hSBA-MenW-135, $\geq 1:4$, M13 [N=123;53] | 123 | 53 | | |
| hSBA-MenW-135, $\geq 1:4$, M14 [N=129;59] | 129 | 59 | | |
| hSBA-MenY, $\geq 1:4$, M13 [N=138;61] | 137 | 60 | | |
| hSBA-MenY, $\geq 1:4$, M14 [N=149;69] | 149 | 69 | | |
| hSBA-MenA, $\geq 1:8$, M13 [N=152;71] | 130 | 47 | | |
| hSBA-MenA, $\geq 1:8$, M14 [N=173;83] | 173 | 83 | | |
| hSBA-MenC, $\geq 1:8$, M13 [N=173;78] | 168 | 75 | | |
| hSBA-MenC, $\geq 1:8$, M14 [N=198;92] | 198 | 92 | | |
| hSBA-MenW-135, $\geq 1:8$, M13 [N=123;53] | 123 | 53 | | |
| hSBA-MenW-135, $\geq 1:8$, M14 [N=129;59] | 129 | 59 | | |
| hSBA-MenY, $\geq 1:8$, M13 [N=138;61] | 137 | 60 | | |
| hSBA-MenY, $\geq 1:8$, M14 [N=149;69] | 149 | 69 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-Men-Y antibody titers at month 13 and 14

| | |
|-----------------|---|
| End point title | hSBA-MenA, hSBA-MenC, hSBA-MenW-135, and hSBA-Men-Y |
|-----------------|---|

End point description:

Antibody titers are presented as geometric mean titers (GMTs).

End point type Secondary

End point timeframe:

At Month 13 (pre-booster for Nimenrix 3+1 and Nimenrix 1+1 Groups and pre-vaccination for Nimenrix Control), and at Month 14 (post-booster for Nimenrix 3+1 and Nimenrix 1+1 Groups and post-vaccination for Nimenrix Control)

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: Not all arms in the Baseline Period are applicable for this endpoint.

| End point values | Nimenrix 3+1 Group | Nimenrix 1+1 Group | | |
|--|------------------------------|------------------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 198 | 92 | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| hSBA-MenA, M13 [N=152;71] | 64.6 (48.8 to 85.5) | 20.8 (13.5 to 32.2) | | |
| hSBA-MenA, M14 [N=173;83] | 2318.6 (1991.7 to 2699.1) | 1415.6 (1140.2 to 1757.5) | | |
| hSBA-MenC, M13 [N=173;78] | 209.0 (165.7 to 263.7) | 150.8 (108.5 to 209.5) | | |
| hSBA-MenC, M14 [N=198;92] | 15919.1 (13965.3 to 18146.2) | 13360.1 (10952.9 to 16296.4) | | |
| hSBA-MenW-135, M13 [N=123;53] | 307.9 (262.9 to 360.6) | 428.6 (328.4 to 559.2) | | |
| hSBA-MenW-135, M14 [N=129;59] | 8761.8 (7431.3 to 10330.5) | 9015.6 (7045.2 to 11537.1) | | |
| hSBA-MenY, M13 [N=138;61] | 363.2 (309.9 to 425.7) | 389.2 (292.3 to 518.1) | | |
| hSBA-MenY, M14 [N=149;69] | 5989.3 (5281.0 to 6792.6) | 5977.6 (4746.8 to 7527.6) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with booster responses for hSBA-MenA, hSBA-MenC, hSBA-MenW-135 and hSBA-MenY in Nimenrix 3+1 and Nimenrix 1+1 Groups and With Vaccine Response in Nimenrix 1 Group

| | |
|-----------------|---|
| End point title | Number of subjects with booster responses for hSBA-MenA, hSBA-MenC, hSBA-MenW-135 and hSBA-MenY in Nimenrix 3+1 and Nimenrix 1+1 Groups and With Vaccine Response in Nimenrix 1 Group |
|-----------------|---|

End point description:

Booster response defined as: for seronegative subjects, antibody titre $\geq 1:8$ at post-booster vaccination; for seropositive subjects, antibody titre at post-booster vaccination ≥ 4 -fold the pre-booster vaccination antibody titre; for initially seropositive subjects: antibody titre at M14 ≥ 4 fold the pre-

vaccination antibody titre.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| At Month 14 (one month after the booster dose in Nimenrix 3+1 and Nimenrix 1+1 and post-vaccination in Nimenrix 1 Group) | |

| End point values | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix 1 Group | |
|------------------------------------|--------------------|--------------------|------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 163 | 75 | 65 | |
| Units: Participants | | | | |
| hSBA-MenA, Total [N=137;64;58] | 130 | 61 | 51 | |
| hSBA-MenC, Total [N=163;75;65] | 163 | 73 | 65 | |
| hSBA-MenW-135, Total [N=107;42;38] | 106 | 40 | 37 | |
| hSBA-MenY, Total [N=122;49;34] | 115 | 45 | 30 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-pneumococcal antibody concentrations greater than or equal to (\geq) 0.15 micrograms per millilitre ($\mu\text{g/mL}$).

| | |
|-----------------|--|
| End point title | Number of subjects with anti-pneumococcal antibody concentrations greater than or equal to (\geq) 0.15 micrograms per millilitre ($\mu\text{g/mL}$). |
|-----------------|--|

End point description:

The anti-pneumococcal serotypes assessed were 1, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F.

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

End point timeframe:

At Month 5 (one month post-dose 3), Month 13 (prior booster dose) and Month 14 (one month after the booster dose)

| End point values | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix Control Group | |
|-----------------------------|--------------------|--------------------|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 82 | 42 | 37 | |
| Units: Participants | | | | |
| anti-1, M5 [N=82;42;37] | 82 | 42 | 37 | |
| anti-1, M13 [N=57;32;27] | 36 | 19 | 19 | |
| anti-1, M14 [N=61;30;29] | 61 | 29 | 29 | |
| anti-4, M5 [N=82;42;37] | 82 | 42 | 37 | |
| anti-4, M13 [N=57;33;27] | 38 | 22 | 20 | |
| anti-4, M14 [N=61;30;29] | 61 | 30 | 29 | |
| anti-5, M5 [N=82;42;37] | 81 | 42 | 37 | |
| anti-5, M13 [N=57;33;27] | 32 | 18 | 17 | |
| anti-5, M14 [N=61;30;29] | 60 | 29 | 27 | |

| | | | | |
|----------------------------|----|----|----|--|
| anti-6A, M5 [N=69;37;28] | 51 | 31 | 22 | |
| anti-6A, M13 [N=56;32;26] | 44 | 26 | 16 | |
| anti-6A, M14 [N=51;25;25] | 51 | 25 | 24 | |
| anti-6B, M5 [N=81;42;37] | 81 | 41 | 37 | |
| anti-6B, M13 [N=57;33;27] | 55 | 31 | 22 | |
| anti-6B, M14 [N=61;30;29] | 61 | 30 | 28 | |
| anti-7F, M5 [N=82;42;37] | 82 | 42 | 37 | |
| anti-7F, M13 [N=57;33;27] | 55 | 32 | 23 | |
| anti-7F, M14 [N=61;30;29] | 61 | 29 | 29 | |
| anti-9V, M5 [N=82;42;37] | 82 | 42 | 37 | |
| anti-9V, M13 [N=57;33;27] | 47 | 24 | 17 | |
| anti-9V, M14 [N=61;30;29] | 61 | 29 | 29 | |
| anti-14, M5 [N=82;42;36] | 82 | 42 | 36 | |
| anti-14, M13 [N=57;33;27] | 56 | 33 | 25 | |
| anti-14, M14 [N=61;30;29] | 61 | 30 | 29 | |
| anti-18C, M5 [N=82;42;37] | 81 | 42 | 37 | |
| anti-18C, M13 [N=57;33;27] | 43 | 20 | 19 | |
| anti-18C, M14 [N=61;30;29] | 61 | 29 | 29 | |
| anti-19A, M5 [N=82;42;37] | 49 | 26 | 27 | |
| anti-19A, M13 [N=57;33;27] | 41 | 23 | 20 | |
| anti-19A, M14 [N=61;29;29] | 57 | 27 | 27 | |
| anti-19F, M5 [N=81;42;37] | 81 | 42 | 36 | |
| anti-19F, M13 [N=57;33;27] | 57 | 33 | 25 | |
| anti-19F, M14 [N=61;30;29] | 61 | 30 | 29 | |
| anti-23F, M5 [N=71;42;36] | 66 | 42 | 35 | |
| anti-23F, M13 [N=57;33;26] | 42 | 25 | 18 | |
| anti-23F, M14 [N=45;24;21] | 45 | 23 | 21 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-pneumococcal antibody concentrations greater than or equal to (\geq) 0.35 micrograms per millilitre ($\mu\text{g/mL}$)

| | |
|-----------------|---|
| End point title | Number of subjects with anti-pneumococcal antibody concentrations greater than or equal to (\geq) 0.35 micrograms per millilitre ($\mu\text{g/mL}$) |
|-----------------|---|

End point description:

The anti-pneumococcal serotypes assessed were 1, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F.

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

End point timeframe:

At Month 5 (one month post-dose 3), Month 13 (prior booster dose) and Month 14 (one month after the booster dose)

| End point values | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix Control Group | |
|-----------------------------|--------------------|--------------------|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 82 | 42 | 37 | |
| Units: Participants | | | | |
| anti-1, M5 [N=82;42;37] | 76 | 41 | 34 | |
| anti-1, M13 [N=57;32;27] | 12 | 5 | 8 | |
| anti-1, M14 [N=61;30;29] | 61 | 29 | 28 | |
| anti-4, M5 [N=82;42;37] | 81 | 41 | 37 | |
| anti-4, M13 [N=57;33;27] | 17 | 5 | 10 | |
| anti-4, M14 [N=61;30;29] | 58 | 29 | 29 | |
| anti-5, M5 [N=82;42;37] | 72 | 32 | 28 | |
| anti-5, M13 [N=57;33;27] | 10 | 5 | 5 | |
| anti-5, M14 [N=61;30;29] | 49 | 23 | 26 | |
| anti-6A, M5 [N=69;37;28] | 36 | 20 | 13 | |
| anti-6A, M13 [N=56;32;26] | 26 | 10 | 11 | |
| anti-6A, M14 [N=51;25;25] | 47 | 22 | 23 | |
| anti-6B, M5 [N=81;42;37] | 73 | 40 | 35 | |
| anti-6B, M13 [N=57;33;27] | 37 | 23 | 15 | |
| anti-6B, M14 [N=61;30;29] | 61 | 28 | 28 | |
| anti-7F, M5 [N=82;42;37] | 81 | 42 | 37 | |
| anti-7F, M13 [N=57;33;27] | 38 | 17 | 14 | |
| anti-7F, M14 [N=61;30;29] | 61 | 29 | 28 | |
| anti-9V, M5 [N=82;42;37] | 79 | 40 | 36 | |
| anti-9V, M13 [N=57;33;27] | 19 | 10 | 9 | |
| anti-9V, M14 [N=61;30;29] | 59 | 28 | 28 | |
| anti-14, M5 [N=82;42;36] | 80 | 41 | 36 | |
| anti-14, M13 [N=57;33;27] | 44 | 28 | 21 | |
| anti-14, M14 [N=61;30;29] | 61 | 29 | 28 | |
| anti-18C, M5 [N=82;42;37] | 79 | 41 | 36 | |
| anti-18C, M13 [N=57;33;27] | 18 | 9 | 11 | |
| anti-18C, M14 [N=61;30;29] | 61 | 27 | 29 | |
| anti-19A, M5 [N=82;42;37] | 28 | 14 | 13 | |
| anti-19A, M13 [N=57;33;27] | 25 | 15 | 5 | |
| anti-19A, M14 [N=61;29;29] | 52 | 21 | 22 | |
| anti-19F, M5 [N=81;42;37] | 80 | 42 | 36 | |
| anti-19F, M13 [N=57;33;27] | 52 | 30 | 20 | |
| anti-19F, M14 [N=61;30;29] | 61 | 30 | 29 | |
| anti-23F, M5 [N=71;42;36] | 62 | 42 | 32 | |
| anti-23F, M13 [N=57;33;26] | 28 | 14 | 12 | |
| anti-23F, M14 [N=45;24;21] | 45 | 23 | 20 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-pneumococcal antibody concentrations

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

End point description:

Antibody concentrations were expressed as Geometric Mean Concentrations (GMCs) and measured in micrograms/millilitre (µg/mL)

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

End point timeframe:

At Month 5 (one month post-dose 3), Month 13 (prior booster-dose) and Month 14 (one month after the booster dose)

| End point values | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix Control Group | |
|--|--------------------|--------------------|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 82 | 42 | 37 | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| anti-1, M5 [N=82;42;37] | 1.3 (1.1 to 1.6) | 1.4 (1.1 to 1.8) | 1.5 (1.1 to 2.1) | |
| anti-1, M13 [N=57;32;27] | 0.2 (0.1 to 0.2) | 0.2 (0.1 to 0.2) | 0.2 (0.2 to 0.3) | |
| anti-1, M14 [N=61;30;29] | 2.1 (1.6 to 2.6) | 1.7 (1.2 to 2.5) | 2.2 (1.5 to 3.2) | |
| anti-4, M5 [N=82;42;37] | 1.7 (1.5 to 2.0) | 1.8 (1.4 to 2.2) | 1.8 (1.3 to 2.5) | |
| anti-4, M13 [N=57;33;27] | 0.2 (0.2 to 0.3) | 0.2 (0.2 to 0.3) | 0.3 (0.2 to 0.4) | |
| anti-4, M14 [N=61;30;29] | 2.4 (1.8 to 3.1) | 2.4 (1.8 to 3.1) | 3.1 (2.3 to 4.2) | |
| anti-5, M5 [N=82;42;37] | 0.6 (0.6 to 0.7) | 0.6 (0.5 to 0.7) | 0.7 (0.5 to 0.9) | |
| anti-5, M13 [N=57;33;27] | 0.2 (0.1 to 0.2) | 0.2 (0.1 to 0.2) | 0.2 (0.1 to 0.2) | |
| anti-5, M14 [N=61;30;29] | 0.7 (0.6 to 0.9) | 0.5 (0.4 to 0.7) | 0.7 (0.5 to 1.0) | |
| anti-6A, M5 [N=69;37;28] | 0.3 (0.3 to 0.4) | 0.4 (0.3 to 0.6) | 0.3 (0.2 to 0.4) | |
| anti-6A, M13 [N=56;32;26] | 0.3 (0.2 to 0.4) | 0.3 (0.2 to 0.4) | 0.2 (0.2 to 0.4) | |
| anti-6A, M14 [N=51;25;25] | 1.7 (1.3 to 2.3) | 1.4 (0.9 to 2.1) | 1.6 (1.0 to 2.5) | |
| anti-6B, M5 [N=81;42;37] | 1.8 (1.4 to 2.3) | 1.7 (1.3 to 2.4) | 1.8 (1.3 to 2.5) | |
| anti-6B, M13 [N=57;33;27] | 0.6 (0.4 to 0.7) | 0.5 (0.4 to 0.7) | 0.4 (0.3 to 0.7) | |
| anti-6B, M14 [N=61;30;29] | 3.8 (3.1 to 4.8) | 2.4 (1.7 to 3.5) | 3.4 (2.2 to 5.2) | |
| anti-7F, M5 [N=82;42;37] | 2.5 (2.2 to 3.0) | 2.2 (1.8 to 2.7) | 2.8 (2.1 to 3.7) | |
| anti-7F, M13 [N=57;33;27] | 0.4 (0.4 to 0.5) | 0.4 (0.3 to 0.5) | 0.4 (0.3 to 0.6) | |
| anti-7F, M14 [N=61;30;29] | 3.5 (2.9 to 4.2) | 2.2 (1.6 to 3.1) | 3.4 (2.4 to 4.9) | |
| anti-9V, M5 [N=82;42;37] | 1.2 (1.0 to 1.4) | 1.2 (1.0 to 1.5) | 1.3 (1.0 to 1.7) | |
| anti-9V, M13 [N=57;33;27] | 0.3 (0.2 to 0.4) | 0.3 (0.2 to 0.4) | 0.2 (0.1 to 0.3) | |
| anti-9V, M14 [N=61;30;29] | 1.6 (1.3 to 2.0) | 1.0 (0.8 to 1.4) | 1.6 (1.2 to 2.2) | |
| anti-14, M5 [N=82;42;36] | 5.2 (4.1 to 6.5) | 6.0 (4.4 to 8.0) | 7.0 (4.9 to 10.0) | |
| anti-14, M13 [N=57;33;27] | 1.0 (0.7 to 1.3) | 0.8 (0.6 to 1.0) | 0.9 (0.5 to 1.4) | |
| anti-14, M14 [N=61;30;29] | 8.4 (6.8 to 10.4) | 6.8 (4.8 to 9.7) | 9.0 (6.0 to 13.5) | |
| anti-18C, M5 [N=82;42;37] | 2.3 (1.9 to 2.8) | 2.0 (1.5 to 2.5) | 2.9 (2.2 to 3.8) | |
| anti-18C, M13 [N=57;33;27] | 0.2 (0.2 to 0.3) | 0.2 (0.1 to 0.3) | 0.3 (0.2 to 0.4) | |
| anti-18C, M14 [N=61;30;29] | 3.6 (3.0 to 4.4) | 2.3 (1.5 to 3.6) | 3.4 (2.6 to 4.6) | |
| anti-19A, M5 [N=82;42;37] | 0.2 (0.2 to 0.3) | 0.2 (0.2 to 0.4) | 0.2 (0.2 to 0.3) | |
| anti-19A, M13 [N=57;33;27] | 0.3 (0.2 to 0.4) | 0.3 (0.2 to 0.4) | 0.2 (0.1 to 0.3) | |
| anti-19A, M14 [N=61;29;29] | 1.2 (0.8 to 1.7) | 1.1 (0.6 to 1.9) | 0.8 (0.5 to 1.2) | |
| anti-19F, M5 [N=81;42;37] | 3.7 (3.0 to 4.6) | 3.8 (2.7 to 5.3) | 4.7 (3.3 to 6.6) | |
| anti-19F, M13 [N=57;33;27] | 0.9 (0.7 to 1.2) | 0.9 (0.7 to 1.3) | 0.9 (0.5 to 1.5) | |
| anti-19F, M14 [N=61;30;29] | 8.0 (6.2 to 10.2) | 6.9 (4.5 to 10.6) | 9.8 (6.8 to 14.2) | |

| | | | | |
|----------------------------|------------------|------------------|------------------|--|
| anti-23F, M5 [N=71;42;36] | 1.4 (1.0 to 1.9) | 1.8 (1.4 to 2.4) | 1.5 (1.0 to 2.2) | |
| anti-23F, M13 [N=57;33;26] | 0.3 (0.2 to 0.4) | 0.3 (0.2 to 0.4) | 0.2 (0.2 to 0.4) | |
| anti-23F, M14 [N=45;24;21] | 3.4 (2.6 to 4.5) | 2.1 (1.3 to 3.4) | 2.9 (1.8 to 4.7) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-diphtheria (anti-D) antibodies, by ATP cohort

| | |
|-----------------|--|
| End point title | Number of subjects with anti-diphtheria (anti-D) antibodies, by ATP cohort |
|-----------------|--|

End point description:

Cut-off values assessed were greater than or equal to (\geq) 0.1 international units per millilitre (IU/mL). The analysis was performed in a randomized subset of 25% of subjects of all three groups.

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

End point timeframe:

At Month 5 (one month post dose 3)

| End point values | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix Control Group | |
|-----------------------------|--------------------|--------------------|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 72 | 34 | 38 | |
| Units: Participants | | | | |
| Participants | 72 | 34 | 38 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of antibodies against diphtheria antigens (anti-D), by ATP cohort

| | |
|-----------------|---|
| End point title | Concentration of antibodies against diphtheria antigens (anti-D), by ATP cohort |
|-----------------|---|

End point description:

Concentrations are presented as geometric mean concentrations (GMCs) expressed in international units per millilitre (IU/mL). The analysis was performed in a randomized subset of 25% of subjects of all three groups.

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

End point timeframe:

At Month 5 (one month post dose 3)

| End point values | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix Control Group | |
|--|------------------------|------------------------|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 72 | 34 | 38 | |
| Units: IU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| IU/mL | 2.259 (1.820 to 2.804) | 3.028 (2.177 to 4.213) | 2.462 (1.700 to 3.565) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-diphtheria (anti-D) antibodies, by TVC

| | |
|-----------------|---|
| End point title | Number of subjects with anti-diphtheria (anti-D) antibodies, by TVC |
|-----------------|---|

End point description:

Cut-off values assessed were greater than or equal to (\geq) 0.1 international units per millilitre (IU/mL). The analysis was performed in a randomized subset of 25% of subjects of all three groups. Note: As the percentage of subjects with serological results excluded from the ATP cohorts was higher than 5%, a second analysis based on the total vaccinated cohorts (TVCs) (Primary and Booster) was performed to complement the ATP analysis.

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

End point timeframe:

At Month 5 (one month post dose 3)

| End point values | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix Control Group | |
|-----------------------------|--------------------|--------------------|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 76 | 36 | 39 | |
| Units: Participants | | | | |
| Participants | 76 | 36 | 39 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of antibodies against diphtheria antigens (anti-D), by TVC

| | |
|-----------------|--|
| End point title | Concentration of antibodies against diphtheria antigens (anti-D), by TVC |
|-----------------|--|

End point description:

Concentrations are presented as geometric mean concentrations (GMCs) expressed in international units per millilitre (IU/mL). The analysis was performed in a randomized subset of 25% of subjects of all three groups. Note: As the percentage of subjects with serological results excluded from the ATP cohorts was higher than 5%, a second analysis based on the total vaccinated cohorts (TVCs) (Primary and Booster) was performed to complement the ATP analysis.

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

End point timeframe:

At Month 5 (one month post dose 3)

| End point values | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix Control Group | |
|--|------------------------|------------------------|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 76 | 36 | 39 | |
| Units: IU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| IU/mL | 2.435 (1.958 to 3.028) | 3.069 (2.225 to 4.233) | 2.423 (1.688 to 3.479) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA), anti-pertactin (anti-PRN) Immunoglobulin G (IgG) antibodies, by ATP cohort

| | |
|-----------------|---|
| End point title | Number of subjects with anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA), anti-pertactin (anti-PRN) Immunoglobulin G (IgG) antibodies, by ATP cohort |
|-----------------|---|

End point description:

Cut-off values assessed were greater than or equal to ≥ 5 enzyme-linked immunosorbent assay (ELISA) units per millilitre (EL.U/ml). The analysis was performed in a randomized subset of 25% of subjects of all three groups.

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

End point timeframe:

At Month 5 (one month post dose 3)

| End point values | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix Control Group | |
|-----------------------------|--------------------|--------------------|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 73 | 34 | 39 | |
| Units: Participants | | | | |
| anti-PT, M5 | 73 | 34 | 39 | |
| anti-FHA, M5 | 73 | 34 | 39 | |
| anti-PRN, M5 | 73 | 34 | 38 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of antibodies against pertussis toxoid (anti-PT), filamentous haemagglutinin (anti-FHA), pertactin (anti-PRN) antigens, by ATP cohort

| | |
|-----------------|---|
| End point title | Concentration of antibodies against pertussis toxoid (anti-PT), filamentous haemagglutinin (anti-FHA), pertactin (anti-PRN) antigens, by ATP cohort |
|-----------------|---|

End point description:

Concentrations are presented as geometric mean concentrations (GMCs) expressed in enzyme-linked immunosorbent assay (ELISA) units per millilitre (EL.U/ml).

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

End point timeframe:

At Month 5 (one month post dose 3)

| End point values | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix Control Group | |
|--|------------------------|------------------------|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 73 | 34 | 39 | |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| anti-PT, M5 | 49.9 (43.3 to 57.6) | 51.9 (40.8 to 66.0) | 47.8 (38.3 to 59.7) | |
| anti-FHA, M5 | 126.2 (108.8 to 146.3) | 134.2 (108.3 to 166.4) | 132.6 (107.8 to 163.1) | |
| anti-PRN, M5 | 108.6 (88.8 to 132.9) | 167.5 (117.6 to 238.7) | 158.2 (106.5 to 235.1) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA), anti-pertactin (anti-PRN) Immunoglobulin G (IgG) antibodies, by TVC

| | |
|-----------------|--|
| End point title | Number of subjects with anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA), anti-pertactin (anti-PRN) Immunoglobulin G (IgG) antibodies, by TVC |
|-----------------|--|

End point description:

Cut-off values assessed were greater than or equal to ≥ 5 enzyme-linked immunosorbent assay (ELISA) units per millilitre (EL.U/ml). The analysis was performed in a randomized subset of 25% of subjects of all three groups. Note: As the percentage of subjects with serological results excluded from the ATP cohorts was higher than 5%, a second analysis based on the total vaccinated cohorts (TVCs) (Primary and Booster) was performed to complement the ATP analysis.

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

End point timeframe:

At Month 5 (one month post dose 3)

| End point values | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix Control Group | |
|-----------------------------|--------------------|--------------------|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 77 | 36 | 40 | |
| Units: Participants | | | | |
| anti-PT, M5 | 77 | 36 | 40 | |
| anti-FHA, M5 | 77 | 36 | 40 | |
| anti-PRN, M5 | 77 | 36 | 39 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of antibodies against pertussis toxoid (anti-PT), filamentous haemagglutinin (anti-FHA), pertactin (anti-PRN) antigens, by TVC

| | |
|-----------------|--|
| End point title | Concentration of antibodies against pertussis toxoid (anti-PT), filamentous haemagglutinin (anti-FHA), pertactin (anti-PRN) antigens, by TVC |
|-----------------|--|

End point description:

Concentrations are presented as geometric mean concentrations (GMCs) expressed in enzyme-linked immunosorbent assay (ELISA) units per millilitre (EL.U/ml) Note: As the percentage of subjects with serological results excluded from the ATP cohorts was higher than 5%, a second analysis based on the total vaccinated cohorts (TVCs) (Primary and Booster) was performed to complement the ATP analysis.

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

End point timeframe:

At Month 5 (one month post dose 3)

| End point values | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix Control Group | |
|--|------------------------|------------------------|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 77 | 36 | 40 | |
| Units: EL.U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| anti-PT, M5 | 50.4 (43.9 to 57.8) | 54.7 (42.9 to 69.9) | 46.4 (37.0 to 58.1) | |
| anti-FHA, M5 | 127.3 (110.6 to 146.6) | 143.3 (114.4 to 179.4) | 129.4 (105.1 to 159.2) | |
| anti-PRN, M5 | 116.7 (95.2 to 143.1) | 178.9 (125.5 to 255.1) | 154.8 (105.0 to 228.3) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-poliovirus type 1, 2 and 3 antibodies, by ATP cohort

| | |
|-----------------|---|
| End point title | Number of subjects with anti-poliovirus type 1, 2 and 3 |
|-----------------|---|

End point description:

Cut-off values assessed were greater than or equal to (\geq) 1:8 titers. The analysis was performed in a randomized subset of 25% of subjects of all three groups.

End point type Secondary

End point timeframe:

At Month 5 (one month post dose 3)

| End point values | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix Control Group | |
|-------------------------------|--------------------|--------------------|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 69 | 29 | 33 | |
| Units: Participants | | | | |
| anti-Polio 1, M5 [N=69;28;29] | 69 | 28 | 29 | |
| anti-Polio 2, M5 [N=69;29;33] | 69 | 29 | 33 | |
| anti-Polio 3, M5 [N=68;26;30] | 68 | 26 | 30 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody titers for anti-polio type 1, 2 and 3 antibodies, by ATP cohort

End point title Antibody titers for anti-polio type 1, 2 and 3 antibodies, by ATP cohort

End point description:

Antibody titers are presented as geometric mean titers (GMTs). The analysis was performed in a randomized subset of 25% of subjects of all three groups.

End point type Secondary

End point timeframe:

At Month 5 (one month post dose 3)

| End point values | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix Control Group | |
|--|---------------------------|---------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 69 | 29 | 33 | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| anti-Polio 1, M5 [N=69;28;29] | 788.8 (584.1 to 1065.2) | 1102.9 (725.2 to 1677.2) | 908.6 (549.1 to 1503.4) | |
| anti-Polio 2, M5 [N=69;29;33] | 850.4 (647.3 to 1117.3) | 953.3 (579.0 to 1569.5) | 1079.2 (704.9 to 1652.1) | |
| anti-Polio 3, M5 [N=68;26;30] | 1678.8 (1211.2 to 2326.9) | 1676.7 (1011.1 to 2780.5) | 1261.3 (720.8 to 2207.1) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-poliovirus type 1, 2 and 3 antibodies, by TVC

| | |
|--|--|
| End point title | Number of subjects with anti-poliovirus type 1, 2 and 3 antibodies, by TVC |
| End point description: Cut-off values assessed were greater than or equal to (\geq) 1:8 titers. The analysis was performed in a randomized subset of 25% of subjects of all three groups. Note: As the percentage of subjects with serological results excluded from the ATP cohorts was higher than 5%, a second analysis based on the total vaccinated cohorts (TVCs) (Primary and Booster) was performed to complement the ATP analysis. | |
| End point type | Secondary |
| End point timeframe: At Month 5 (one month post dose 3) | |

| End point values | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix Control Group | |
|-------------------------------|--------------------|--------------------|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 73 | 31 | 34 | |
| Units: Participants | | | | |
| anti-Polio 1, M5 [N=73;30;30] | 73 | 30 | 30 | |
| anti-Polio 2, M5 [N=73;31;34] | 73 | 31 | 34 | |
| anti-Polio 3, M5 [N=71;28;31] | 71 | 28 | 31 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody titers for anti-polio type 1, 2 and 3 antibodies, by TVC

| | |
|--|---|
| End point title | Antibody titers for anti-polio type 1, 2 and 3 antibodies, by TVC |
| End point description: Antibody titers are presented as geometric mean titers (GMTs). The analysis was performed in a randomized subset of 25% of subjects of all three groups. Note: As the percentage of subjects with serological results excluded from the ATP cohorts was higher than 5%, a second analysis based on the total vaccinated cohorts (TVCs) (Primary and Booster) was performed to complement the ATP analysis. | |
| End point type | Secondary |
| End point timeframe: At Month 5 (one month post dose 3) | |

| End point values | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix Control Group | |
|--|---------------------------|--------------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 73 | 31 | 34 | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| anti-Polio 1, M5 [N=73;30;30] | 827.2 (618.7 to 1105.8) | 1048.1 (681.1 to 1612.7) | 861.0 (523.3 to 1416.8) | |
| anti-Polio 2, M5 [N=73;31;34] | 931.3 (707.7 to 1225.6) | 990.4 (606.5 to 1617.3) | 1024.0 (668.6 to 1568.2) | |
| anti-Polio 3, M5 [N=71;28;31] | 1709.5 (1245.4 to 2346.7) | 1618.7 (963.7 to 2719.0) | 1184.8 (679.9 to 2064.4) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-tetanus (anti-T) antibodies, by ATP

| | |
|--|--|
| End point title | Number of subjects with anti-tetanus (anti-T) antibodies, by ATP |
| End point description: | |
| Cut-off values assessed were greater than or equal to (\geq) 0.1 international units per millilitre (IU/mL). The analysis was performed in a randomized subset of 25% of subjects of all three groups. | |
| End point type | Secondary |
| End point timeframe: | |
| At Month 5 (one month post-dose 3), Month 13 (prior booster-dose) and Month 14 (one month after the booster dose) | |

| End point values | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix Control Group | |
|-----------------------------|--------------------|--------------------|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 77 | 36 | 40 | |
| Units: Participants | | | | |
| anti-T, M5 [N=77;36;40] | 77 | 36 | 40 | |
| anti-T, M13 [N=59;29;26] | 58 | 28 | 24 | |
| anti-T, M14 [N=62;22;23] | 62 | 22 | 23 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of antibodies against tetanus antigens (anti-T), by ATP

| | |
|-----------------|---|
| End point title | Concentration of antibodies against tetanus antigens (anti-T), by ATP |
|-----------------|---|

End point description:

Concentrations are presented as geometric mean concentrations (GMCs) expressed in international units per millilitre (IU/mL). The analysis was performed in a randomized subset of 25% of subjects of all three groups.

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

End point timeframe:

At Month 5 (one month post-dose 3), Month 13 (prior booster-dose) and Month 14 (one month after the booster dose)

| End point values | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix Control Group | |
|--|---------------------------|---------------------------|---------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 73 | 34 | 39 | |
| Units: IU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| anti-T, M5 [N=73, 34, 39] | 5.798 (4.998 to 6.726) | 7.246 (5.305 to 9.897) | 5.973 (4.818 to 7.406) | |
| anti-T, M13 [N=49, 24,21] | 0.479 (0.398 to 0.576) | 0.659 (0.427 to 1.018) | 0.461 (0.297 to 0.716) | |
| anti-T, M14 [N=57,20,21] | 18.977 (16.013 to 22.489) | 16.813 (12.386 to 22.821) | 35.835 (23.802 to 53.951) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Concentration of antibodies against tetanus antigens (anti-T), by TVC

| | |
|-----------------|---|
| End point title | Concentration of antibodies against tetanus antigens (anti-T), by TVC |
|-----------------|---|

End point description:

Concentrations are presented as geometric mean concentrations (GMCs) expressed in international units per millilitre (IU/mL). The analysis was performed in a randomized subset of 25% of subjects of all three groups. Note: As the percentage of subjects with serological results excluded from the ATP cohorts was higher than 5%, a second analysis based on the total vaccinated cohorts (TVCs) (Primary and Booster) was performed to complement the ATP analysis.

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

End point timeframe:

At Month 5 (one month post-dose 3), 13 (prior booster-dose) and 14 (one month after the booster dose)

| End point values | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix Control Group | |
|--|---------------------------|---------------------------|---------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 77 | 36 | 40 | |
| Units: IU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| anti-T, M5 [N=77;36;40] | 6.099 (5.236 to 7.104) | 7.402 (5.510 to 9.943) | 5.901 (4.780 to 7.286) | |
| anti-T, M13 [N=58;29;24] | 0.535 (0.450 to 0.636) | 0.610 (0.414 to 0.899) | 0.419 (0.287 to 0.610) | |
| anti-T, M14 [N=40;26;23] | 18.889 (16.158 to 22.082) | 16.809 (12.710 to 22.230) | 36.593 (25.224 to 53.085) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-tetanus (anti-T) antibodies, by TVC

| | |
|-----------------|--|
| End point title | Number of subjects with anti-tetanus (anti-T) antibodies, by TVC |
|-----------------|--|

End point description:

Cut-off values assessed were greater than or equal to (\geq) 0.1 international units per millilitre (IU/mL). The analysis was performed in a randomized subset of 25% of subjects of all three groups. Note: As the percentage of subjects with serological results excluded from the ATP cohorts was higher than 5%, a second analysis based on the total vaccinated cohorts (TVCs) (Primary and Booster) was performed to complement the ATP analysis.

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

End point timeframe:

At Month 5 (one month post-dose 3), Month 13 (prior booster-dose) and Month 14 (one month after the booster dose)

| End point values | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix Control Group | |
|-----------------------------|--------------------|--------------------|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 77 | 36 | 40 | |
| Units: Participants | | | | |
| anti-T, M5 [N=77;36;40] | 77 | 36 | 40 | |
| anti-T, M13 [N=58;29;24] | 58 | 28 | 24 | |
| anti-T, 14 [N=40;26;23] | 62 | 22 | 23 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-PRP antibody concentrations (Geometric Mean Concentrations) in a randomized subset of 25% of the subjects

| | |
|---|--|
| End point title | Anti-PRP antibody concentrations (Geometric Mean Concentrations) in a randomized subset of 25% of the subjects |
| End point description: The endpoints evaluating immunogenicity of the Hib component (anti-polyribosyl ribitol phosphate [anti-PRP] antibody concentrations) has been cancelled owing to the extended delay in the re-development and re-validation of the PRP assay. | |
| End point type | Secondary |
| End point timeframe: At Month 5 (one month post-dose 3) | |

| End point values | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix Control Group | |
|--|--------------------|--------------------|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 0 ^[12] | 0 ^[13] | 0 ^[14] | |
| Units: µg/mL | | | | |
| geometric mean (confidence interval 95%) | (to) | (to) | (to) | |

Notes:

[12] - No subjects were analyzed because the Hib component immunogenicity assessment was cancelled.

[13] - No subjects were analyzed because the Hib component immunogenicity assessment was cancelled.

[14] - No subjects were analyzed because the Hib component immunogenicity assessment was cancelled.

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited local symptoms (Primary Phase)

| | |
|---|--|
| End point title | Number of subjects with solicited local symptoms (Primary Phase) |
| End point description: Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = pain that prevented normal activity. Grade 3 redness/swelling = redness/swelling spreading beyond 30 millimeters (mm) of injection site. | |
| End point type | Secondary |
| End point timeframe: Within 8 days (Day 0-7) post primary vaccination | |

| End point values | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix Control Group | |
|--|--------------------|--------------------|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 369 | 182 | 184 | |
| Units: Participants | | | | |
| Any Pain Dose 1 [N=369;182;184] | 220 | 115 | 108 | |
| Grade 3 Pain Dose 1 [N=369;182;184] | 38 | 25 | 14 | |
| Any Redness Dose 1 [N=369;182;184] | 94 | 39 | 43 | |
| Grade 3 Redness Dose 1 [N=369;182;184] | 1 | 0 | 0 | |
| Any Swelling Dose 1 [N=369;182;184] | 84 | 31 | 34 | |

| | | | | |
|--|-----|-----|-----|--|
| Grade 3 Swelling Dose 1 [N=369;182;184] | 0 | 3 | 0 | |
| Any Pain Dose 2 [N=363;181;181] | 177 | 92 | 101 | |
| Grade 3 Pain Dose 2 [N=363;181;181] | 33 | 11 | 16 | |
| Any Redness Dose 2 [N=363;181;181] | 93 | 51 | 48 | |
| Grade 3 Redness Dose 2 [N=363;181;181] | 2 | 0 | 1 | |
| Any Swelling Dose 2 [N=363;181;181] | 76 | 47 | 42 | |
| Grade 3 Swelling Dose 2 [N=363;181;181] | 2 | 2 | 0 | |
| Any Pain Dose 3 [N=359;177;180] | 148 | 73 | 93 | |
| Grade 3 Pain Dose 3 [N=359;177;180] | 16 | 18 | 9 | |
| Any Redness Dose 3 [N=359;177;180] | 74 | 46 | 42 | |
| Grade 3 Redness Dose 3 [N=359;177;180] | 1 | 1 | 1 | |
| Any Swelling Dose 3 [N=359;177;180] | 66 | 46 | 37 | |
| Grade 3 Swelling Dose 3 [N=359;177;180] | 1 | 0 | 0 | |
| Any Pain Across Doses [N=369;182;184] | 262 | 135 | 142 | |
| Grade 3 Pain Across Doses [N=369;182;184] | 65 | 36 | 33 | |
| Any Redness Across Doses [N=369;182;184] | 160 | 79 | 78 | |
| Grade 3 Redness Across Doses [N=369;182;184] | 4 | 1 | 2 | |
| Any Swelling Across Doses [N=369;182;184] | 147 | 74 | 70 | |
| Grade 3 Swelling Across Doses [N=369;182;184] | 3 | 4 | 0 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited local symptoms (Booster Phase)

| | |
|-----------------|--|
| End point title | Number of subjects with solicited local symptoms (Booster Phase) |
|-----------------|--|

End point description:

Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = pain that prevented normal activity. Grade 3 redness/swelling = redness/swelling spreading beyond 30 millimeters (mm) of injection site.

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

End point timeframe:

Within 8 days (Day 0-7) post booster vaccination

| End point values | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix 1 Group | |
|-----------------------------|--------------------|--------------------|------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 338 | 165 | 167 | |
| Units: Participants | | | | |
| Any Pain | 139 | 71 | 77 | |
| Grade 3 Pain | 21 | 19 | 14 | |
| Any Redness | 74 | 32 | 39 | |
| Grade 3 Redness | 1 | 1 | 3 | |
| Any Swelling | 55 | 29 | 33 | |
| Grade 3 Swelling | 2 | 1 | 3 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited general symptoms (Primary Phase)

| | |
|-----------------|--|
| End point title | Number of subjects with solicited general symptoms (Primary Phase) |
|-----------------|--|

End point description:

Assessed solicited general symptoms were temperature [defined as rectally temperature equal to or above 38 degrees Celsius (°C)], drowsiness, irritability and loss of appetite. Any = occurrence of the symptom regardless of intensity grade. Grade 3 symptom = symptom that prevented normal activity. Grade 3 temperature = temperature > 40.0 °C. Related = symptom assessed by the investigator as related to the vaccination.

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

End point timeframe:

Within 8 days (Day 0-7) post primary vaccination

| End point values | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix Control Group | |
|---|--------------------|--------------------|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 369 | 182 | 184 | |
| Units: Participants | | | | |
| Any Drowsiness Dose 1 [N=369;182;184] | 177 | 93 | 84 | |
| Grade 3 Drowsiness Dose 1 [N=369;182;184] | 18 | 10 | 2 | |
| Related Drowsiness Dose 1 [N=369;182;184] | 160 | 84 | 79 | |
| Any Irritability Dose 1 [N=369;182;184] | 200 | 107 | 99 | |
| Grade 3 Irritability Dose 1 [N=369;182;184] | 19 | 9 | 10 | |
| Related Irritability Dose 1 [N=369;182;184] | 188 | 96 | 89 | |
| Any Loss of appetite Dose 1 [N=369;182;184] | 109 | 62 | 42 | |
| Grade 3 Loss of appetite Dose 1 [N=369;182;184] | 7 | 5 | 3 | |
| Related Loss of appetite Dose 1 [N=369;182;184] | 99 | 55 | 35 | |

| | | | | |
|--|-----|-----|-----|--|
| Any Temperature Dose 1 [N=369;182;184] | 126 | 62 | 58 | |
| Grade 3 Temperature Dose 1 [N=369;182;184] | 0 | 0 | 1 | |
| Related Temperature Dose 1 [N=369;182;184] | 109 | 56 | 53 | |
| Any Drowsiness Dose 2 [N=363;181;181] | 116 | 72 | 67 | |
| Grade 3 Drowsiness Dose 2 [N=363;181;181] | 9 | 8 | 8 | |
| Related Drowsiness Dose 2 [N=363;181;181] | 109 | 69 | 62 | |
| Any Irritability Dose 2 [N=363;181;181] | 163 | 82 | 90 | |
| Grade 3 Irritability Dose 2 [N=363;181;181] | 20 | 14 | 10 | |
| Related Irritability Dose 2 [N=363;181;181] | 158 | 77 | 85 | |
| Any Loss of appetite Dose 2 [N=363;181;181] | 89 | 50 | 44 | |
| Grade 3 Loss of appetite Dose 2 [N=363;181;181] | 6 | 5 | 6 | |
| Related Loss of appetite Dose 2 [N=363;181;181] | 80 | 48 | 39 | |
| Any Temperature Dose 2 [N=363;181;181] | 119 | 64 | 63 | |
| Grade 3 Temperature Dose 2 [N=363;181;181] | 0 | 0 | 0 | |
| Related Temperature Dose 2 [N=363;181;181] | 116 | 59 | 54 | |
| Any Drowsiness Dose 3 [N=359;177;180] | 102 | 54 | 64 | |
| Grade 3 Drowsiness Dose 3 [N=359;177;180] | 11 | 8 | 4 | |
| Related Drowsiness Dose 3 [N=359;177;180] | 95 | 54 | 60 | |
| Any Irritability Dose 3 [N=359;177;180] | 140 | 73 | 73 | |
| Grade 3 Irritability Dose 3 [N=359;177;180] | 14 | 14 | 3 | |
| Related Irritability Dose 3 [N=359;177;180] | 132 | 72 | 69 | |
| Any Loss of appetite Dose 3 [N=359;177;180] | 76 | 43 | 50 | |
| Grade 3 Loss of appetite Dose 3 [N=359;177;180] | 7 | 6 | 3 | |
| Related Loss of appetite Dose 3 [N=359;177;180] | 63 | 41 | 46 | |
| Any Temperature Dose 3 [N=359;177;180] | 109 | 51 | 41 | |
| Grade 3 Temperature Dose 3 [N=359;177;180] | 2 | 0 | 0 | |
| Related Temperature Dose 3 [N=359;177;180] | 96 | 46 | 36 | |
| Any Drowsiness Across Doses [N=369;182;184] | 217 | 121 | 118 | |
| Grade 3 Drowsiness Across Doses [N=369;182;184] | 30 | 19 | 13 | |
| Related Drowsiness Across Doses [N=369;182;184] | 205 | 116 | 114 | |
| Any Irritability Across Doses [N=369;182;184] | 254 | 128 | 126 | |
| Grade 3 Irritability Across Doses [N=369;182;184] | 42 | 27 | 18 | |

| | | | | |
|--|-----|-----|-----|--|
| Related Irritability Across Doses [N=369;182;184] | 246 | 125 | 121 | |
| Any Loss of appetite Across [N=369;182;184] | 165 | 89 | 82 | |
| Grade 3 Loss of appetite Across [N=369;182;184] | 17 | 13 | 10 | |
| Related Loss of appetite Across [N=369;182;184] | 151 | 84 | 77 | |
| Any Temperature Across Doses [N=369;182;184] | 203 | 102 | 101 | |
| Grade 3 Temperature Across Doses [N=369;182;184] | 2 | 0 | 1 | |
| Related Temperature Across Doses [N=369;182;184] | 193 | 97 | 93 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited general symptoms (Booster Phase)

| | |
|-----------------|--|
| End point title | Number of subjects with solicited general symptoms (Booster Phase) |
|-----------------|--|

End point description:

Assessed solicited general symptoms were temperature [defined as rectally temperature equal to or above 38 degrees Celsius (°C)], drowsiness, irritability and loss of appetite. Any = occurrence of the symptom regardless of intensity grade. Grade 3 symptom = symptom that prevented normal activity. Grade 3 temperature = temperature > 40.0 °C. Related = symptom assessed by the investigator as related to the vaccination.

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

End point timeframe:

Within 8 days (Day 0-7) post booster vaccination

| End point values | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix 1 Group | |
|-----------------------------|-----------------------|-----------------------|---------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 338 | 165 | 167 | |
| Units: Participants | | | | |
| Any Drowsiness | 79 | 46 | 43 | |
| Grade 3 Drowsiness | 4 | 7 | 5 | |
| Related Drowsiness | 75 | 42 | 43 | |
| Any Irritability | 112 | 54 | 61 | |
| Grade 3 Irritability | 9 | 12 | 10 | |
| Related Irritability | 106 | 52 | 60 | |
| Any Loss of appetite | 69 | 37 | 39 | |
| Grade 3 Loss of appetite | 5 | 5 | 1 | |
| Related Loss of appetite | 60 | 34 | 37 | |
| Any Temperature | 68 | 35 | 27 | |
| Grade 3 Temperature | 2 | 1 | 0 | |
| Related Temperature | 62 | 32 | 24 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited adverse events (AEs) (Primary Phase)

| | |
|-----------------|--|
| End point title | Number of subjects with unsolicited adverse events (AEs) (Primary Phase) |
|-----------------|--|

End point description:

An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination.

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

End point timeframe:

Within 31 days (Day 0-30) post each primary vaccine dose

| End point values | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix Control Group | |
|----------------------------------|--------------------|--------------------|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 376 | 187 | 187 | |
| Units: Participants | | | | |
| Any AE(s) Dose 1 [N=376;187;187] | 67 | 36 | 34 | |
| Any AE(s) Dose 2 [N=368;182;182] | 70 | 34 | 28 | |
| Any AE(s) Dose 3 [N=362;179;181] | 97 | 49 | 45 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited adverse events (AEs) (Booster phase)

| | |
|-----------------|--|
| End point title | Number of subjects with unsolicited adverse events (AEs) (Booster phase) |
|-----------------|--|

End point description:

An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination.

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

End point timeframe:

Within 31 days (Day 0-30) post booster vaccination

| End point values | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix 1 Group | |
|-----------------------------|--------------------|--------------------|------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 342 | 166 | 170 | |
| Units: Participants | | | | |
| Participants | 58 | 32 | 36 | |

Statistical analyses

No statistical analyses for this end point

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

| | |
|------------------------|---|
| End point title | Number of subjects with new onset of chronic illnesses (NOCIs) |
| End point description: | NOCIs include autoimmune disorders, asthma, type I diabetes, allergies. |
| End point type | Secondary |
| End point timeframe: | From Day 0 to Month 18 |

| End point values | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix Control Group | |
|-----------------------------|--------------------|--------------------|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 376 | 187 | 187 | |
| Units: Participants | | | | |
| Participants | 16 | 8 | 4 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with serious adverse events (SAEs)

| | |
|------------------------|---|
| End point title | Number of subjects with serious adverse events (SAEs) |
| End point description: | Serious adverse events (SAEs) assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity. |
| End point type | Secondary |
| End point timeframe: | From Day 0 to Month 19 |

| End point values | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix Control Group | |
|-----------------------------|--------------------|--------------------|------------------------|--|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 376 | 187 | 187 | |
| Units: Participants | | | | |
| Participants | 35 | 14 | 14 | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited local/general symptoms during the 8-day post-vaccination period (Days 0-7), Unsolicited AEs during the 31-day post-vaccination (Days 0-30), SAEs during the entire study period (Day 0 - Month 19).

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

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 18.1 |

Reporting groups

| | |
|-----------------------|--------------------|
| Reporting group title | Nimenrix 3+1 Group |
|-----------------------|--------------------|

Reporting group description:

Subjects, male and female, received 4 doses of Nimenrix vaccine (3 doses at 2, 4 and 6 months of age followed by a booster dose at 15-18 months of age) and 4 doses of Synflorix and Infanrix-IPV/Hiberix vaccines (at 2, 4, 6 and 15-18 months of age). All vaccines were administered intramuscularly (IM) in the anterolateral region of the thigh.

| | |
|-----------------------|--------------------|
| Reporting group title | Nimenrix 1+1 Group |
|-----------------------|--------------------|

Reporting group description:

Subjects, male and female, received 2 doses of Nimenrix vaccine (1 dose at 6 months of age followed by a booster dose at 15-18 months of age) and 4 doses of Synflorix and Infanrix-IPV/Hiberix vaccines (at 2, 4, 6 and 15-18 months of age). All vaccines were administered intramuscularly (IM) in the anterolateral region of the thigh.

| | |
|-----------------------|------------------------|
| Reporting group title | Nimenrix Control Group |
|-----------------------|------------------------|

Reporting group description:

Subjects, male and female, received 1 dose of Nimenrix at 15-18 months of age and 4 doses of Synflorix and Infanrix-IPV/Hiberix vaccines (at 2, 4, 6 and 15-18 months of age). All vaccines were administered intramuscularly (IM) in the anterolateral region of the thigh.

| Serious adverse events | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix Control Group |
|---|--------------------|--------------------|------------------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 35 / 376 (9.31%) | 14 / 187 (7.49%) | 14 / 187 (7.49%) |
| number of deaths (all causes) | 0 | 0 | 1 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Burns first degree | | | |
| subjects affected / exposed | 1 / 376 (0.27%) | 0 / 187 (0.00%) | 0 / 187 (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 |
| Burns second degree | | | |
| subjects affected / exposed | 1 / 376 (0.27%) | 0 / 187 (0.00%) | 0 / 187 (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 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Foreign body | | | |
| subjects affected / exposed | 0 / 376 (0.00%) | 0 / 187 (0.00%) | 1 / 187 (0.53%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Head injury | | | |
| subjects affected / exposed | 0 / 376 (0.00%) | 2 / 187 (1.07%) | 0 / 187 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skull fracture | | | |
| subjects affected / exposed | 0 / 376 (0.00%) | 1 / 187 (0.53%) | 0 / 187 (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 |
| Subdural haematoma | | | |
| subjects affected / exposed | 0 / 376 (0.00%) | 1 / 187 (0.53%) | 0 / 187 (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 |
| Toxicity to various agents | | | |
| subjects affected / exposed | 0 / 376 (0.00%) | 0 / 187 (0.00%) | 1 / 187 (0.53%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Epilepsy | | | |
| subjects affected / exposed | 1 / 376 (0.27%) | 0 / 187 (0.00%) | 0 / 187 (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 |
| Febrile convulsion | | | |
| subjects affected / exposed | 1 / 376 (0.27%) | 1 / 187 (0.53%) | 0 / 187 (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 |
| Hyponatraemic seizure | | | |
| subjects affected / exposed | 0 / 376 (0.00%) | 0 / 187 (0.00%) | 1 / 187 (0.53%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Seizure | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 376 (0.00%) | 1 / 187 (0.53%) | 1 / 187 (0.53%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 2 / 376 (0.53%) | 0 / 187 (0.00%) | 0 / 187 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Sudden infant death syndrome | | | |
| subjects affected / exposed | 0 / 376 (0.00%) | 0 / 187 (0.00%) | 1 / 187 (0.53%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| Immune system disorders | | | |
| Anaphylactic shock | | | |
| subjects affected / exposed | 0 / 376 (0.00%) | 1 / 187 (0.53%) | 0 / 187 (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 |
| Drug hypersensitivity | | | |
| subjects affected / exposed | 1 / 376 (0.27%) | 1 / 187 (0.53%) | 0 / 187 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Milk allergy | | | |
| subjects affected / exposed | 1 / 376 (0.27%) | 0 / 187 (0.00%) | 0 / 187 (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 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 2 / 376 (0.53%) | 0 / 187 (0.00%) | 1 / 187 (0.53%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ileus paralytic | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 376 (0.27%) | 0 / 187 (0.00%) | 0 / 187 (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 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Lung disorder | | | |
| subjects affected / exposed | 1 / 376 (0.27%) | 0 / 187 (0.00%) | 0 / 187 (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 | | | |
| Amoebic dysentery | | | |
| subjects affected / exposed | 0 / 376 (0.00%) | 1 / 187 (0.53%) | 0 / 187 (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 |
| Bronchiolitis | | | |
| subjects affected / exposed | 5 / 376 (1.33%) | 1 / 187 (0.53%) | 3 / 187 (1.60%) |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchitis | | | |
| subjects affected / exposed | 3 / 376 (0.80%) | 0 / 187 (0.00%) | 1 / 187 (0.53%) |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 376 (0.00%) | 0 / 187 (0.00%) | 1 / 187 (0.53%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ear infection | | | |
| subjects affected / exposed | 0 / 376 (0.00%) | 0 / 187 (0.00%) | 1 / 187 (0.53%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Escherichia urinary tract infection | | | |
| subjects affected / exposed | 1 / 376 (0.27%) | 2 / 187 (1.07%) | 0 / 187 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|-----------------|-----------------|-----------------|
| Gastroenteritis | | | |
| subjects affected / exposed | 4 / 376 (1.06%) | 1 / 187 (0.53%) | 3 / 187 (1.60%) |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis rotavirus | | | |
| subjects affected / exposed | 1 / 376 (0.27%) | 0 / 187 (0.00%) | 0 / 187 (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 viral | | | |
| subjects affected / exposed | 2 / 376 (0.53%) | 0 / 187 (0.00%) | 1 / 187 (0.53%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Measles | | | |
| subjects affected / exposed | 1 / 376 (0.27%) | 0 / 187 (0.00%) | 0 / 187 (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 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 376 (0.00%) | 0 / 187 (0.00%) | 2 / 187 (1.07%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Neurological infection | | | |
| subjects affected / exposed | 1 / 376 (0.27%) | 0 / 187 (0.00%) | 0 / 187 (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 |
| Otitis media | | | |
| subjects affected / exposed | 0 / 376 (0.00%) | 1 / 187 (0.53%) | 0 / 187 (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 |
| Pharyngitis | | | |
| subjects affected / exposed | 1 / 376 (0.27%) | 1 / 187 (0.53%) | 0 / 187 (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 |
| Pharyngotonsillitis | | | |

| | | | |
|---|------------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 376 (0.27%) | 1 / 187 (0.53%) | 0 / 187 (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 |
| Pneumonia | | | |
| subjects affected / exposed | 13 / 376 (3.46%) | 2 / 187 (1.07%) | 3 / 187 (1.60%) |
| occurrences causally related to treatment / all | 0 / 16 | 0 / 2 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia viral | | | |
| subjects affected / exposed | 1 / 376 (0.27%) | 0 / 187 (0.00%) | 0 / 187 (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 |
| Roseola | | | |
| subjects affected / exposed | 1 / 376 (0.27%) | 0 / 187 (0.00%) | 0 / 187 (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 | 0 / 376 (0.00%) | 1 / 187 (0.53%) | 0 / 187 (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 |
| Urinary tract infection | | | |
| subjects affected / exposed | 2 / 376 (0.53%) | 2 / 187 (1.07%) | 0 / 187 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viral infection | | | |
| subjects affected / exposed | 1 / 376 (0.27%) | 0 / 187 (0.00%) | 0 / 187 (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 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 2 / 376 (0.53%) | 1 / 187 (0.53%) | 1 / 187 (0.53%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | 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 | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix Control Group |
|---|--------------------|--------------------|------------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 334 / 376 (88.83%) | 169 / 187 (90.37%) | 169 / 187 (90.37%) |
| Nervous system disorders | | | |
| Somnolence | | | |
| subjects affected / exposed | 224 / 376 (59.57%) | 124 / 187 (66.31%) | 120 / 187 (64.17%) |
| occurrences (all) | 475 | 265 | 258 |
| General disorders and administration site conditions | | | |
| Pain | | | |
| subjects affected / exposed | 273 / 376 (72.61%) | 142 / 187 (75.94%) | 145 / 187 (77.54%) |
| occurrences (all) | 684 | 351 | 379 |
| Pyrexia | | | |
| subjects affected / exposed | 215 / 376 (57.18%) | 112 / 187 (59.89%) | 111 / 187 (59.36%) |
| occurrences (all) | 426 | 214 | 192 |
| Swelling | | | |
| subjects affected / exposed | 157 / 376 (41.76%) | 83 / 187 (44.39%) | 78 / 187 (41.71%) |
| occurrences (all) | 281 | 153 | 146 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 36 / 376 (9.57%) | 15 / 187 (8.02%) | 10 / 187 (5.35%) |
| occurrences (all) | 38 | 16 | 10 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 23 / 376 (6.12%) | 8 / 187 (4.28%) | 5 / 187 (2.67%) |
| occurrences (all) | 25 | 8 | 5 |
| Skin and subcutaneous tissue disorders | | | |
| Erythema | | | |
| subjects affected / exposed | 177 / 376 (47.07%) | 87 / 187 (46.52%) | 87 / 187 (46.52%) |
| occurrences (all) | 335 | 168 | 172 |
| Psychiatric disorders | | | |
| Irritability | | | |
| subjects affected / exposed | 262 / 376 (69.68%) | 130 / 187 (69.52%) | 130 / 187 (69.52%) |
| occurrences (all) | 616 | 316 | 323 |
| Infections and infestations | | | |

| | | | |
|--|---------------------------|--------------------------|--------------------------|
| Nasopharyngitis subjects affected / exposed occurrences (all) | 65 / 376 (17.29%) 83 | 27 / 187 (14.44%) 42 | 26 / 187 (13.90%) 35 |
| Pharyngitis subjects affected / exposed occurrences (all) | 39 / 376 (10.37%) 42 | 17 / 187 (9.09%) 25 | 27 / 187 (14.44%) 32 |
| Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all) | 185 / 376 (49.20%) 343 | 95 / 187 (50.80%) 192 | 95 / 187 (50.80%) 175 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|--------------|--|
| 26 July 2011 | <p>Amendment 1</p> <p>One of the participating countries has requested that the subjects enrolled in that country be vaccinated with acellualr pertussis vaccine instead of whole cell pertussis vaccine in order to align with the national recommendation. On account of this request the following changes have been made in the protocol as part of this amendment.</p> <ul style="list-style-type: none">• All subjects will be co-administrated with Infanrix-IPV/Hiberix instead of Tritanrix-HepB/Hiberix that was foreseen in the original protocol. Consequently, changes have been made in the exclusion and elimination criteria, assays, secondary endpoints and the statistical analysis section.- HepB, and whole cell pertussis assays have been removed and assays for the evaluation of acellular pertussis and polio type 1, 2 and 3 have been included.- Secondary endpoints and the statistical analysis sections have been modified to remove whole cell pertussis and HepB analysis and to include acellular pertussis and polio type 1, 2 and 3 analysis.- Exclusion and elimination criteria have been revised based on the change in the co-administered vaccines• Subjects will receive both primary and booster doses of Infanrix- IPV/Hiberix• Interval during which concomitant vaccinations are allowed has been clarified in the exclusion and elimination criteria to ensure that no concomitant vaccination is given during the period between a study vaccine administration and the subsequent blood sampling visit, if applicable. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported