# 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 | |

**Results information**

| | |
|---|---|
| Result version number | v1 |
| This version publication date | 29 April 2016 |
| First version publication date | 29 April 2016 |

## 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, 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 | Interim |
| Date of interim/final analysis | 12 April 2016 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 04 August 2014 |
| Global end of trial reached? | 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 ≥ 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 months) | 753 |

| | |
|---|---|
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

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

### Period 1

| | |
|---|---|
| Period 1 title | 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 who received 3 doses of Nimenrix™ vaccine at 3 doses at 2, 4 and 6 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 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 who received 1 dose of Nimenrix vaccine 1 dose at 6 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 6 months of age.

| 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 | 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.

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

Arm description:

Subjects who received routine administration of Infanrix-IPV, Hiberix and Synflorix at 2, 4 and 6 months of age.

| Arm type | Active comparator |
|---|---|

| | |
|---|---|
| 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 | 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.

| **Number of subjects in period 1[1]** | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix 1 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 | - |
| Serious adverse event | - | - | 1 |
| Lost to follow-up | 4 | 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 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 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 | 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.

| | |
|---|---|
| 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.

| | |
|---|---|
| **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.

| | |
|---|---|
| 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.

| **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 who received 3 doses of Nimenrix™ vaccine at 3 doses at 2, 4 and 6 months of age. | |
| Reporting group title | Nimenrix 1+1 Group |
| Reporting group description: | |
| Subjects who received 1 dose of Nimenrix vaccine 1 dose at 6 months of age. | |
| Reporting group title | Nimenrix 1 Group |
| Reporting group description: | |
| Subjects who received routine administration of Infanrix-IPV, Hiberix and Synflorix at 2, 4 and 6 months of age. | |

| Reporting group values | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix 1 Group |
|---|---|---|---|
| Number of subjects | 376 | 187 | 187 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | | |
| Preterm newborn infants (gestational age < 37 wks) | | | |
| Newborns (0-27 days) | | | |
| Infants and toddlers (28 days-23 months) | | | |
| Children (2-11 years) | | | |
| Adolescents (12-17 years) | | | |
| Adults (18-64 years) | | | |
| From 65-84 years | | | |
| 85 years and over | | | |
| Age continuous | | | |
| Units: months | | | |
| 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 |

| Reporting group values | Total | | |
|---|---|---|---|
| Number of subjects | 750 | | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | 0 | | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | | |
| Newborns (0-27 days) | 0 | | |
| Infants and toddlers (28 days-23 months) | 0 | | |
| Children (2-11 years) | 0 | | |
| Adolescents (12-17 years) | 0 | | |

| | | | |
|---|---|---|---|
| Adults (18-64 years) | 0 | | |
| From 65-84 years | 0 | | |
| 85 years and over | 0 | | |
| Age continuous | | | |
| Units: months | | | |
| arithmetic mean | | | |
| standard deviation | - | | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 382 | | |
| Male | 368 | | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Nimenrix 3+1 Group |
| Reporting group description: | |
| Subjects who received 3 doses of Nimenrix™ vaccine at 3 doses at 2, 4 and 6 months of age. | |
| Reporting group title | Nimenrix 1+1 Group |
| Reporting group description: | |
| Subjects who received 1 dose of Nimenrix vaccine 1 dose at 6 months of age. | |
| Reporting group title | Nimenrix 1 Group |
| Reporting group description: | |
| Subjects who received routine administration of Infanrix-IPV, Hiberix and Synflorix at 2, 4 and 6 months of age. | |
| Reporting group title | Nimenrix 3+1 Group |
| Reporting group description: | |
| Subjects who received 1 dose of Nimenrix™ vaccine at 15-18 months of age. | |
| Reporting group title | Nimenrix 1+1 Group |
| Reporting group description: | |
| Subjects who received 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 meningococcal polysaccharide A serum bactericidal assay using baby rabbit complement (rSBA-MenA) titers ≥ 1:8

| | |
|---|---|
| End point title | Number of subjects with meningococcal polysaccharide A serum bactericidal assay using baby rabbit complement (rSBA-MenA) titers ≥ 1:8[1] |
| End point description: | |
| | |
| End point type | Primary |
| End point timeframe: | |
| One month following 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: Results will be updated when they become available.

| 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 | 0[2] | 0[3] | 0[4] | |
| Units: Subjects | | | | |
| rSBA-MenA, D3 | | | | |

Notes:

[2] - Immunogenicity results will be updated when they become available.

[3] - Immunogenicity results will be updated when they become available.

[4] - Immunogenicity results will be updated when they become available.

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with solicited local symptoms (PRI)

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

End point description:

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

End point timeframe:

Withing 8 days (Day 0-7) post primary 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 | 369 | 182 | 184 | |
| Units: Subjects | | | | |
| 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 (BST)

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

End point description:

| 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: Subjects | | | | |
| 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 (PRI)

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

End point description:

| 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 1 Group | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | |
| Number of subjects analysed | 369 | 182 | 184 | |
| Units: Subjects | | | | |
| 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 (BST)

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

End point description:

| 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: Subjects | | | | |
| 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) (PRI)

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

End point description:

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

End point timeframe:

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

| 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 | 376 | 187 | 187 | |
| Units: Subjects | | | | |
| 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) (BST)

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

End point description:

| 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: Subjects | | | | |
| Any AE(s) | 58 | 32 | 36 | |

**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:

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

End point timeframe:

During the entire study period

| **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 | 376 | 187 | 187 | |
| Units: Subjects | | | | |
| Any SAE(s) | 35 | 14 | 14 | |

**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:

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

End point timeframe:

During the entire study period

| **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 | 376 | 187 | 187 | |
| Units: Subjects | | | | |
| Any NOCI(s) | 16 | 8 | 4 | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: | |
| Solicited symptoms: within 8 days (Day 0-Day 7), AEs: within 31 days (Day 0 – Day 30), SAEs: throughout the study period. | |
| 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 who receive 3 primary doses of the investigational vaccine at 2, 4 and 6 months of age and 1 booster dose at 15-18 months of age | |
| Reporting group title | Nimenrix 1+1 Group |
| Reporting group description: | |
| Subjects received 1 primary vaccination dose of the investigational vaccine at 6 months of age and 1 booster dose at 15-18 months of age | |
| Reporting group title | Nimenrix 1 Group |
| Reporting group description: | |
| Subjects received 1 dose of the investigational vaccine at 15-18 months of age | |

| Serious adverse events | Nimenrix 3+1 Group | Nimenrix 1+1 Group | Nimenrix 1 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 | | | |
| Injury, poisoning and procedural complications | | | |
| 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 |
| 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 |
| 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 | | | |
| 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 |
| 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 |
| 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 |
| 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 |
| 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 | | | |
| 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 |
| 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 |
| 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 | | | |
| 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 |
| 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 |
| 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 |
| 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 |
| 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 |
| 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 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 |
| 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 |
| 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 |
| 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 |
| 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 |
| 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 |
| 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 |
| 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 |
| 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 |
| 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 1 Group |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 262 / 376 (69.68%) | 135 / 187 (72.19%) | 142 / 187 (75.94%) |
| General disorders and administration site conditions | | | |
| Pain (Primary) | | | |
| subjects affected / exposed[1] | 262 / 369 (71.00%) | 135 / 182 (74.18%) | 142 / 184 (77.17%) |
| occurrences (all) | 262 | 135 | 142 |
| Redness (Primary) | | | |
| subjects affected / exposed[2] | 160 / 369 (43.36%) | 79 / 182 (43.41%) | 78 / 184 (42.39%) |
| occurrences (all) | 160 | 79 | 78 |
| Swelling (Primary) | | | |
| subjects affected / exposed[3] | 147 / 369 (39.84%) | 74 / 182 (40.66%) | 70 / 184 (38.04%) |
| occurrences (all) | 147 | 74 | 70 |
| Pain (Booster) | | | |
| subjects affected / exposed[4] | 139 / 338 (41.12%) | 71 / 165 (43.03%) | 77 / 167 (46.11%) |
| occurrences (all) | 139 | 71 | 77 |
| Redness (Booster) | | | |
| subjects affected / exposed[5] | 74 / 338 (21.89%) | 32 / 165 (19.39%) | 39 / 167 (23.35%) |
| occurrences (all) | 74 | 32 | 39 |
| Swelling (Booster) | | | |
| subjects affected / exposed[6] | 55 / 338 (16.27%) | 29 / 165 (17.58%) | 33 / 167 (19.76%) |
| occurrences (all) | 55 | 29 | 33 |
| Drowsiness (Primary) | | | |
| subjects affected / exposed[7] | 217 / 369 (58.81%) | 121 / 182 (66.48%) | 118 / 184 (64.13%) |
| occurrences (all) | 217 | 121 | 118 |
| Irritability (Primary) | | | |
| subjects affected / exposed[8] | 254 / 369 (68.83%) | 128 / 182 (70.33%) | 126 / 184 (68.48%) |
| occurrences (all) | 254 | 128 | 126 |
| Loss of appetite (Primary) | | | |
| subjects affected / exposed[9] | 165 / 369 (44.72%) | 89 / 182 (48.90%) | 82 / 184 (44.57%) |
| occurrences (all) | 165 | 89 | 82 |
| Temperature(Rectally) (Primary) | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed[10] | 203 / 369 (55.01%) | 102 / 182 (56.04%) | 101 / 184 (54.89%) |
| occurrences (all) | 203 | 102 | 101 |
| Drowsiness (Booster) | | | |
| subjects affected / exposed[11] | 79 / 338 (23.37%) | 46 / 165 (27.88%) | 43 / 167 (25.75%) |
| occurrences (all) | 79 | 46 | 43 |
| Irritability (Booster) | | | |
| subjects affected / exposed[12] | 112 / 338 (33.14%) | 54 / 165 (32.73%) | 61 / 167 (36.53%) |
| occurrences (all) | 112 | 54 | 61 |
| Loss of appetite (Booster) | | | |
| subjects affected / exposed[13] | 69 / 338 (20.41%) | 37 / 165 (22.42%) | 39 / 167 (23.35%) |
| occurrences (all) | 69 | 37 | 39 |
| Temperature(Rectally) (Booster) | | | |
| subjects affected / exposed[14] | 68 / 338 (20.12%) | 35 / 165 (21.21%) | 27 / 167 (16.17%) |
| occurrences (all) | 68 | 35 | 27 |
| Infections and infestations | | | |
| Nasopharyngitis (Booster) | | | |
| subjects affected / exposed[15] | 17 / 342 (4.97%) | 12 / 166 (7.23%) | 7 / 170 (4.12%) |
| occurrences (all) | 17 | 12 | 7 |
| Nasopharyngitis (Primary) | | | |
| subjects affected / exposed[16] | 31 / 362 (8.56%) | 14 / 179 (7.82%) | 10 / 181 (5.52%) |
| occurrences (all) | 31 | 14 | 10 |
| Pharyngitis | | | |
| subjects affected / exposed[17] | 17 / 362 (4.70%) | 13 / 179 (7.26%) | 12 / 181 (6.63%) |
| occurrences (all) | 17 | 13 | 12 |

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.
[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.
[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.
[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.
[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
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[11] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
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[12] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.
[13] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
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[14] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
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[15] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
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[16] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.
[17] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The analysis was performed on the Total vaccinated cohort, only on subjects with their symptom sheets completed.

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 26 July 2011 | Amendment 1<br>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.<br>• 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.<br>- 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.<br>- 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.<br>- Exclusion and elimination criteria have been revised based on the change in the co-administered vaccines<br>• Subjects will receive both primary and booster doses of Infanrix-IPV/Hiberix<br>• 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