# Clinical trial results:
# A Phase IIIb, open, randomized study to evaluate non-inferiority of GSK Biologicals' measles-mumps-rubella-varicella vaccine versus co-administration of GSK Biologicals' Priorix™ and Varilrix™ in healthy children during their second year of life

## Summary

| | |
|---|---|
| EudraCT number | 2011-004485-15 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 27 May 2010 |

**Results information**

| | |
|---|---|
| Result version number | v2 (current) |
| This version publication date | 31 May 2023 |
| First version publication date | 30 July 2015 |
| Version creation reason | • Correction of full data set<br>Correction of full data set and alignment between registries. |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | 110876 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00751348 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

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

Notes:

**Paediatric regulatory details**

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

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 15 October 2010 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 27 May 2010 |
| Global end of trial reached? | Yes |
| Global end of trial date | 27 May 2010 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To demonstrate the non-inferiority of GSK Biologicals' combined measles-mumps-rubella-varicella (MeMuRu-Oka) vaccine to Priorix and Varilrix vaccines administered as concomitant, separate injections in terms of measles, mumps, rubella, and varicella zoster virus (VZV) seroconversion rates 42-56 days after vaccination.

Protection of trial subjects:

The subjects were observed closely for at least 30 minutes following the administration of vaccine(s), with appropriate medical treatment readily available in case of a rare anaphylactic reaction.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 16 October 2008 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Korea, Republic of: 474 |
| Worldwide total number of subjects | 474 |
| 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) | 474 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

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

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Priorix-Tetra Group |

Arm description:

Healthy male and female subjects between, and including 11 and 24 months of age, who received one dose of Priorix-Tetra vaccine at Day 0, administered subcutaneously in the deltoid region of the left upper arm.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Priorix-Tetra |
| Investigational medicinal product code | |
| Other name | MMRV |
| Pharmaceutical forms | Powder and solvent for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

One dose of Priorix-Tetra vaccine was administered in the deltoid region of the left upper arm at Day 0.

| | |
|---|---|
| **Arm title** | Priorix + Varilrix Group |

Arm description:

Healthy male and female subjects between, and including 11 and 24 months of age, who received one dose of Priorix vaccine together with one dose of Varilrix vaccine at Day 0, administered subcutaneously in the deltoid regions of the left or right upper arm, respectively.

| | |
|---|---|
| Arm type | Active comparator |
| Investigational medicinal product name | Priorix |
| Investigational medicinal product code | |
| Other name | MMR |
| Pharmaceutical forms | Powder and solvent for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

One dose of Priorix vaccine was administered in the deltoid region of the left upper arm at Day 0.

| | |
|---|---|
| Investigational medicinal product name | Varilrix |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Powder and solvent for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

One dose of Varilrix vaccine was administered in the deltoid region of the right upper arm at Day 0.

| **Number of subjects in period 1** | Priorix-Tetra Group | Priorix + Varilrix Group |
|---|---|---|
| Started | 313 | 161 |
| Completed | 307 | 159 |
| Not completed | 6 | 2 |
| Consent withdrawn by subject | 5 | 2 |
| Migration from study area | 1 | - |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Priorix-Tetra Group |
| Reporting group description: | |
| Healthy male and female subjects between, and including 11 and 24 months of age, who received one dose of Priorix-Tetra vaccine at Day 0, administered subcutaneously in the deltoid region of the left upper arm. | |
| Reporting group title | Priorix + Varilrix Group |
| Reporting group description: | |
| Healthy male and female subjects between, and including 11 and 24 months of age, who received one dose of Priorix vaccine together with one dose of Varilrix vaccine at Day 0, administered subcutaneously in the deltoid regions of the left or right upper arm, respectively. | |

| Reporting group values | Priorix-Tetra Group | Priorix + Varilrix Group | Total |
|---|---|---|---|
| Number of subjects | 313 | 161 | 474 |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | 0 |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | 0 |
| Newborns (0-27 days) | 0 | 0 | 0 |
| Infants and toddlers (28 days-23 months) | 313 | 161 | 474 |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 0 | 0 | 0 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Age continuous<br>Units: months | | | |
| arithmetic mean | 12.4 | 12.5 | |
| standard deviation | ± 1.4 | ± 1.65 | - |
| Gender categorical<br>Units: Subjects | | | |
| Female | 128 | 76 | 204 |
| Male | 185 | 85 | 270 |
| Race/Ethnicity<br>Units: Subjects | | | |
| Asian-East Asian Heritage | 313 | 159 | 472 |
| Asian-South East Asian Heritage | 0 | 2 | 2 |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Priorix-Tetra Group |
| Reporting group description: | |
| Healthy male and female subjects between, and including 11 and 24 months of age, who received one dose of Priorix-Tetra vaccine at Day 0, administered subcutaneously in the deltoid region of the left upper arm. | |
| Reporting group title | Priorix + Varilrix Group |
| Reporting group description: | |
| Healthy male and female subjects between, and including 11 and 24 months of age, who received one dose of Priorix vaccine together with one dose of Varilrix vaccine at Day 0, administered subcutaneously in the deltoid regions of the left or right upper arm, respectively. | |

### Primary: Number of subjects seroconverted for measles, mumps, rubella and varicella zoster virus (VZV) antibodies above the cut-off values

| | |
|---|---|
| End point title | Number of subjects seroconverted for measles, mumps, rubella and varicella zoster virus (VZV) antibodies above the cut-off values |
| End point description: | |
| Seroconversion was defined as the appearance of antibodies [i.e. titer greater than or equal to (≥) the cut-off value] in the sera of subjects seronegative [i.e. titer below (<) cut-off value] before vaccination. Cut-off values were the following: Anti-measles concentration ≥ 150 milli-international units per milliliter (mIU/mL); Anti-mumps concentration ≥ 231 units per milliliter (U/mL); Anti-rubella concentration ≥ 4 international units per milliliter (IU/mL); Anti-VZV titer ≥ 1:4 dilution. | |
| End point type | Primary |
| End point timeframe: | |
| At 42 days post-vaccination | |

| End point values | Priorix-Tetra Group | Priorix + Varilrix Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 300 | 157 | | |
| Units: Subjects | | | | |
| Anti-Measles (N=300; 156) | 294 | 155 | | |
| Anti-Mumps (N=295; 154) | 262 | 145 | | |
| Anti-Rubella (N=298; 157) | 297 | 157 | | |
| Anti-VZV (N=283; 151) | 280 | 151 | | |

### Statistical analyses

| | |
|---|---|
| **Statistical analysis title** | Non-inferiority - vaccine response to anti-measles |
| Statistical analysis description: | |
| Non-inferiority of Priorix-Tetra vaccine vs Priorix and Varilrix administered as concomitant vaccine 42-56 days after vaccination at Day 0 in terms of anti-measles seroconversion rates. | |
| Comparison groups | Priorix-Tetra Group v Priorix + Varilrix Group |

| | |
|---|---|
| Number of subjects included in analysis | 457 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[1] |
| P-value | < 0.05 [2] |
| Method | Fisher exact |
| Parameter estimate | Difference in percentage |
| Point estimate | -1.36 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.77 |
| upper limit | 1.66 |
| Variability estimate | Standard deviation |

Notes:

[1] - Criterion for evaluation of non-inferiority: the lower limit (LL) of the two-sided standardized asymptotic 95% confidence interval (CI) for the group difference (Priorix-Tetra Group minus Priorix+Varilrix Group) in seroconversion rate for anti-measles was above -10%.
[2] - The P-value for all reactogenicity comparisons was below (<) 0.05.

| **Statistical analysis title** | Non-inferiority - vaccine response to anti-mumps |
|---|---|

Statistical analysis description:

Non-inferiority of Priorix-Tetra vaccine vs Priorix and Varilrix administered as concomitant vaccine 42-56 days after vaccination at Day 0 in terms of anti-mumps seroconversion rates.

| | |
|---|---|
| Comparison groups | Priorix-Tetra Group v Priorix + Varilrix Group |
| Number of subjects included in analysis | 457 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[3] |
| P-value | < 0.05 [4] |
| Method | Fisher exact |
| Parameter estimate | Difference in percentage |
| Point estimate | -5.34 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -10.4 |
| upper limit | 0.38 |
| Variability estimate | Standard deviation |

Notes:

[3] - Criterion for evaluation of non-inferiority: the lower limit (LL) of the two-sided standardized asymptotic 95% confidence interval (CI) for the group difference (Priorix-Tetra Group minus Priorix+Varilrix Group) in seroconversion rate for anti-mumps was above -10%.
[4] - The P-value for all reactogenicity comparisons was below (<) 0.05.

| **Statistical analysis title** | Non-inferiority - vaccine response to anti-rubella |
|---|---|

Statistical analysis description:

Non-inferiority of Priorix-Tetra vaccine vs Priorix and Varilrix administered as concomitant vaccine 42-56 days after vaccination at Day 0 in terms of anti-rubella seroconversion rates.

| | |
|---|---|
| Comparison groups | Priorix-Tetra Group v Priorix + Varilrix Group |

| | |
|---|---|
| Number of subjects included in analysis | 457 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[5] |
| P-value | < 0.05 [6] |
| Method | Fisher exact |
| Parameter estimate | Difference in percentage |
| Point estimate | -0.34 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -1.88 |
| upper limit | 2.06 |
| Variability estimate | Standard deviation |

Notes:

[5] - Criterion for evaluation of non-inferiority: the lower limit (LL) of the two-sided standardized asymptotic 95% confidence interval (CI) for the group difference (Priorix-Tetra Group minus Priorix+Varilrix Group) in seroconversion rate for anti-rubella was above -10%.
[6] - The P-value for all reactogenicity comparisons was below (<) 0.05.

| **Statistical analysis title** | Non-inferiority - vaccine response to anti-VZV |
|---|---|

Statistical analysis description:

Non-inferiority of Priorix-Tetra vaccine vs Priorix and Varilrix administered as concomitant vaccine 42-56 days after vaccination at Day 0 in terms of anti-varicella zoster virus (anti-VZV) seroconversion rates.

| | |
|---|---|
| Comparison groups | Priorix-Tetra Group v Priorix + Varilrix Group |
| Number of subjects included in analysis | 457 |
| Analysis specification | Pre-specified |
| Analysis type | non-inferiority[7] |
| P-value | < 0.05 [8] |
| Method | Fisher exact |
| Parameter estimate | Difference in percentage |
| Point estimate | -1.06 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.07 |
| upper limit | 1.44 |
| Variability estimate | Standard deviation |

Notes:

[7] - Criterion for evaluation of non-inferiority: the lower limit (LL) of the two-sided standardized asymptotic 95% confidence interval (CI) for the group difference (Priorix-Tetra Group minus Priorix+Varilrix Group) in seroconversion rate for anti-VZV was above -10%.
[8] - The P-value for all reactogenicity comparisons was below (<) 0.05.

## Secondary: Antibody concentrations against measles

| | |
|---|---|
| End point title | Antibody concentrations against measles |

End point description:

Antibody concentrations were presented as geometric mean concentrations (GMCs), expressed in milli-international units per milliliter (mIU/mL).

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

End point timeframe:

At 42-days post-vaccination

| End point values | Priorix-Tetra Group | Priorix + Varilrix Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 300 | 156 | | |
| Units: mIU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-Measles (N=300; 156) | 4978.6 (4579.8 to 5412.1) | 3433.6 (3116.3 to 3783.2) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Antibody concentrations against mumps

| End point title | Antibody concentrations against mumps |
|---|---|

End point description:

Antibody concentrations were presented as geometric mean concentrations (GMCs), expressed in units per milliliter (U/mL).

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

End point timeframe:

At 42-days post-vaccination

| End point values | Priorix-Tetra Group | Priorix + Varilrix Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 295 | 154 | | |
| Units: U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-Mumps (N=295; 154) | 1012.3 (894.4 to 1145.7) | 934.3 (805.2 to 1084.1) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Antibody concentrations against rubella

| End point title | Antibody concentrations against rubella |
|---|---|

End point description:

Antibody concentrations were presented as geometric mean concentrations (GMCs), expressed in international units per milliliter (IU/mL).

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

End point timeframe:

At 42 days post-vaccination

| End point values | Priorix-Tetra Group | Priorix + Varilrix Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 298 | 157 | | |
| Units: IU/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-Rubella (N=298; 157) | 63.4 (57.9 to 69.4) | 75.7 (68 to 84.3) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Antibody titers against varicella viruses

| End point title | Antibody titers against varicella viruses |
|---|---|

End point description:

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

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

End point timeframe:

At 42 days post-vaccination

| End point values | Priorix-Tetra Group | Priorix + Varilrix Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 283 | 151 | | |
| Units: Titres | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Anti-VZV (N=283; 151) | 134.1 (117 to 153.7) | 129.2 (109.8 to 152) | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with any and Grade 3 solicited local symptoms

| End point title | Number of subjects with any and Grade 3 solicited local symptoms |
|---|---|

End point description:

Solicited local symptoms assessed were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = Cry when limb was moved/spontaneously painful. Grade 3 redness/swelling = redness/swelling spreading beyond 20 millimeters (mm) of injection site.

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

End point timeframe:

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

| **End point values** | Priorix-Tetra Group | Priorix + Varilrix Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 310 | 159 | | |
| Units: Subjects | | | | |
| Any Pain | 15 | 10 | | |
| Grade 3 Pain | 0 | 0 | | |
| Any Redness | 26 | 21 | | |
| Grade 3 Redness | 0 | 1 | | |
| Any Swelling | 5 | 5 | | |
| Grade 3 Swelling | 0 | 0 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with any, grade 3 and related solicited general symptoms

| End point title | Number of subjects with any, grade 3 and related solicited general symptoms |
|---|---|

End point description:

Solicited general symptoms assessed were fever [defined as rectal temperature ≥38.0 degrees Celsius (°C)], rash, meningism and parotid gland swelling. Any= incidence of the specified symptoms regardless of intensity grade or relationship to study vaccine. Grade 3 fever= rectal temperature above (>) 39.5°C. Grade 3 rash= more than 150 lesions. Grade 3 meningism and parotid gland swelling= meningism/parotid gland swelling symptom which prevented normal everyday activities. Related = general symptom assessed by the investigator as causally related to the vaccination.

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

End point timeframe:

During the 43-day (Days 0-42) post-vaccination period

| **End point values** | Priorix-Tetra Group | Priorix + Varilrix Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 310 | 159 | | |
| Units: Subjects | | | | |
| Any temperature | 202 | 82 | | |
| Grade 3 temperature | 53 | 19 | | |
| Related temperature | 31 | 12 | | |

| | | | | |
|---|---|---|---|---|
| Any Rash | 33 | 16 | | |
| Grade 3 Rash | 0 | 0 | | |
| Related Rash | 3 | 1 | | |
| Any Meningism | 2 | 0 | | |
| Grade 3 Meningism | 0 | 0 | | |
| Related Meningism | 0 | 0 | | |
| Any Parotid gland swelling | 0 | 0 | | |
| Grade 3 Parotid gland swelling | 0 | 0 | | |
| Related Parotid gland swelling | 0 | 0 | | |

### Statistical analyses

No statistical analyses for this end point

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

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

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. Any was defined as an adverse event (AE) reported in addition to those solicited during the clinical study. Any solicited symptom with onset outside the specified period of follow-up for solicited symptoms was reported as an unsolicited adverse event.

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

End point timeframe:

Within the 43-day (Days 0-42) post-vaccination period

| End point values | Priorix-Tetra Group | Priorix + Varilrix Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 313 | 161 | | |
| Units: Subjects | | | | |
| Any AE(s) | 194 | 88 | | |

### 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 resulted in death, were life threatening, required hospitalization or prolongation of hospitalization, resulted in disability/incapacity or was a congenital anomaly/birth defect in the offspring of a study subject.

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

End point timeframe:

During the entire study period (from Day 0 up to Day 43 or Day 57)

| **End point values** | Priorix-Tetra Group | Priorix + Varilrix Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 313 | 161 | | |
| Units: Subjects | | | | |
| Any SAE(s) | 25 | 12 | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Solicited local: during the 4-day (Days 0-3) post-vaccination period. Solicited general symptoms and unsolicited AEs: during the 43-day (Days 0-42) post-vaccination period. SAEs: during the entire study period (from Day 0 up to Day 43 or 57).

Adverse event reporting additional description:

The solicited local and general symptoms were only collected from those subjects who filled in their symptom sheets.
The number of occurrences reported for solicited symptoms, adverse events, and serious adverse events were not available for posting. The number of subjects affected by each specific event was indicated as the number of occurrences.

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

### Dictionary used

| | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 13.0 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Priorix-Tetra Group |

Reporting group description:

Healthy male and female subjects between, and including 11 and 24 months of age, who received one dose of Priorix-Tetra vaccine at Day 0, administered subcutaneously in the deltoid region of the left upper arm.

| | |
|---|---|
| Reporting group title | Priorix + Varilrix Group |

Reporting group description:

Healthy male and female subjects between, and including 11 and 24 months of age, who received one dose of Priorix vaccine together with one dose of Varilrix vaccine at Day 0, administered subcutaneously in the deltoid regions of the left or right upper arm, respectively.

| Serious adverse events | Priorix-Tetra Group | Priorix + Varilrix Group | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 25 / 313 (7.99%) | 12 / 161 (7.45%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | 0 | 0 | |
| Injury, poisoning and procedural complications | | | |
| Road traffic accident | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 161 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Febrile convulsion | | | |
| subjects affected / exposed | 2 / 313 (0.64%) | 0 / 161 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 161 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 1 / 161 (0.62%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Hepatitis | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 1 / 161 (0.62%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Acute tonsillitis | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 161 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchiolitis | | | |
| subjects affected / exposed | 3 / 313 (0.96%) | 2 / 161 (1.24%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchopneumonia | | | |
| subjects affected / exposed | 6 / 313 (1.92%) | 3 / 161 (1.86%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Croup infectious | | | |
| subjects affected / exposed | 2 / 313 (0.64%) | 0 / 161 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 5 / 313 (1.60%) | 6 / 161 (3.73%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 6 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis norovirus | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 161 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis rotavirus | | | |
| subjects affected / exposed | 2 / 313 (0.64%) | 0 / 161 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hand-foot-and-mouth disease | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 1 / 161 (0.62%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Herpangina | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 161 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Otitis media | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 161 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Otitis media acute | | | |
| subjects affected / exposed | 3 / 313 (0.96%) | 1 / 161 (0.62%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pharyngitis | | | |
| subjects affected / exposed | 5 / 313 (1.60%) | 1 / 161 (0.62%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pharyngotonsillitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 4 / 313 (1.28%) | 1 / 161 (0.62%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 1 / 161 (0.62%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rhinitis | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 161 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 1 / 161 (0.62%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral rash | | | |
| subjects affected / exposed | 1 / 313 (0.32%) | 0 / 161 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Hypophagia | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 1 / 161 (0.62%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Iron deficiency | | | |
| subjects affected / exposed | 0 / 313 (0.00%) | 1 / 161 (0.62%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| **Non-serious adverse events** | Priorix-Tetra Group | Priorix + Varilrix Group | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 243 / 313 (77.64%) | 113 / 161 (70.19%) | |
| General disorders and administration site conditions | | | |
| Pain | | | |
| subjects affected / exposed[1] | 15 / 310 (4.84%) | 10 / 159 (6.29%) | |
| occurrences (all) | 15 | 10 | |
| Redness | | | |
| subjects affected / exposed[2] | 26 / 310 (8.39%) | 21 / 159 (13.21%) | |
| occurrences (all) | 26 | 21 | |
| Fever | | | |
| subjects affected / exposed[3] | 202 / 310 (65.16%) | 82 / 159 (51.57%) | |
| occurrences (all) | 202 | 82 | |
| Rash | | | |
| subjects affected / exposed[4] | 33 / 310 (10.65%) | 16 / 159 (10.06%) | |
| occurrences (all) | 33 | 16 | |
| Infections and infestations | | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 63 / 313 (20.13%) | 25 / 161 (15.53%) | |
| occurrences (all) | 63 | 25 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 31 / 313 (9.90%) | 14 / 161 (8.70%) | |
| occurrences (all) | 31 | 14 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 28 / 313 (8.95%) | 13 / 161 (8.07%) | |
| occurrences (all) | 28 | 13 | |
| Pharyngitis | | | |
| subjects affected / exposed | 27 / 313 (8.63%) | 10 / 161 (6.21%) | |
| occurrences (all) | 27 | 10 | |
| Bronchitis | | | |
| subjects affected / exposed | 26 / 313 (8.31%) | 11 / 161 (6.83%) | |
| occurrences (all) | 26 | 11 | |
| Bronchiolitis | | | |
| subjects affected / exposed | 21 / 313 (6.71%) | 11 / 161 (6.83%) | |
| occurrences (all) | 21 | 11 | |
| Pharyngotonsillitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 21 / 313 (6.71%) | 10 / 161 (6.21%) | |
| occurrences (all) | 21 | 10 | |
| Otitis media acute | | | |
| subjects affected / exposed | 13 / 313 (4.15%) | 9 / 161 (5.59%) | |
| occurrences (all) | 13 | 9 | |

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: For the analysis of solicited symptom, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects with documented safety data (i.e. symptom screen/sheet 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: For the analysis of solicited symptom, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects with documented safety data (i.e. symptom screen/sheet 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: For the analysis of solicited symptom, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects with documented safety data (i.e. symptom screen/sheet 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: For the analysis of solicited symptom, missing or non-evaluable measurements were not replaced. Therefore the analysis of the solicited symptoms based on the Total Vaccinated cohort included only subjects with documented safety data (i.e. symptom screen/sheet completed).

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported