



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	<ul style="list-style-type: none">• Correction of full data set Correction of full data set and alignment between registries.

Trial information

Trial identification

Sponsor protocol code	110876
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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
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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
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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
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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			
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			
Units: months			
arithmetic mean	12.4	12.5	
standard deviation	± 1.4	± 1.65	-
Gender categorical			
Units: Subjects			
Female	128	76	204
Male	185	85	270
Race/Ethnicity			
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 (\geq) 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 \geq 150 milli-international units per milliliter (mIU/mL); Anti-mumps concentration \geq 231 units per milliliter (U/mL); Anti-rubella concentration \geq 4 international units per milliliter (IU/mL); Anti-VZV titer \geq 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
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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
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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
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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
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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
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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 ($^{\circ}\text{C}$)], 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)
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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
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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)
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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
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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
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Dictionary used

Dictionary name	MedDRA
Dictionary version	13.0

Reporting groups

Reporting group title	Priorix-Tetra Group
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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
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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