



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	v1
This version publication date	27 April 2016
First version publication date	30 July 2015

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	MMRV Group

Arm description:

Subjects received one dose of MMRV vaccine at Day 0.

Arm type	Experimental
Investigational medicinal product name	Priorix-Tetra
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 MMRV vaccine was administered in the deltoid region of the left upper arm at Day 0.

Arm title	MMR+V Group
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Arm description:

Subjects received one dose of MMR vaccine and one dose of V vaccine at Day 0.

Arm type	Active comparator
Investigational medicinal product name	Priorix™
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 MMR vaccine was administered in the deltoid region of the left upper arm.

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 varicella vaccine was administered in the deltoid region of the right upper arm at Day 0.

Number of subjects in period 1	MMRV Group	MMR+V 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	MMRV Group
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Reporting group description:

Subjects received one dose of MMRV vaccine at Day 0.

Reporting group title	MMR+V Group
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Reporting group description:

Subjects received one dose of MMR vaccine and one dose of V vaccine at Day 0.

Reporting group values	MMRV Group	MMR+V Group	Total
Number of subjects	313	161	474
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	12.4	12.5	
standard deviation	± 1.4	± 1.65	-
Gender categorical			
Units: Subjects			
Female	128	76	204
Male	185	85	270

End points

End points reporting groups

Reporting group title	MMRV Group
Reporting group description: Subjects received one dose of MMRV vaccine at Day 0.	
Reporting group title	MMR+V Group
Reporting group description: Subjects received one dose of MMR vaccine and one dose of V vaccine at Day 0.	

Primary: Number of subjects seroconverted for measles, mumps, rubella, and VZV antibodies above the cut-off values.

End point title	Number of subjects seroconverted for measles, mumps, rubella, and VZV antibodies above the cut-off values.
End point description: Seroconversion was defined as the appearance of antibodies (i.e. titer \geq cut-off value) in the sera of subjects seronegative (i.e. titer < cut-off value) before vaccination. Cut-off values are the following: <ul style="list-style-type: none">• Anti-measles concentration \geq 150 mIU/mL• Anti-mumps concentration \geq 231 U/mL• Anti-rubella concentration \geq 4 IU/mL• Anti-VZV titer \geq 1:4 dilution	
End point type	Primary
End point timeframe: At 42-days after vaccination.	

End point values	MMRV Group	MMR+V 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 MMRV vaccine vs MMR and V administered as concomitant vaccine 42-56 days after vaccination at Day 0 in terms of anti-measles seroconversion rates. Non-inferiority with respect to seroconversion rates for measles 42-56 days after vaccination was concluded if the lower limit of the two-sided standardized asymptotic 95% confidence interval (CI) for the group difference (MMRV Group minus MMR+V Group) in seroconversion rate for anti-measles was above -10%.	
Comparison groups	MMRV Group v MMR+V Group

Number of subjects included in analysis	457
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05 ^[1]
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] - The p-values for all reactogenicity comparisons were calculated using a two-sided Fisher Exact test.

Statistical analysis title	Non-inferiority - vaccine response to anti-mumps
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Statistical analysis description:

Non-inferiority of MMRV vaccine vs MMR and V administered as concomitant vaccine 42-56 days after vaccination at Day 0 in terms of anti-mumps seroconversion rates. Non-inferiority with respect to seroconversion rates for mumps 42-56 days after vaccination was concluded if the lower limit of the two-sided standardized asymptotic 95% confidence interval (CI) for the group difference (MMRV Group minus MMR+V Group) in seroconversion rate for anti-mumps was above -10%.

Comparison groups	MMRV Group v MMR+V Group
Number of subjects included in analysis	457
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05 ^[2]
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:

[2] - The p-values for all reactogenicity comparisons were calculated using a two-sided Fisher Exact test.

Statistical analysis title	Non-inferiority - vaccine response to anti-rubella
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Statistical analysis description:

Non-inferiority of MMRV vaccine vs MMR and V administered as concomitant vaccine 42-56 days after vaccination at Day 0 in terms of of anti-rubella seroconversion rates. Non-inferiority with respect to seroconversion rates for rubella 42-56 days after vaccination was concluded if the lower limit of the two-sided standardized asymptotic 95% confidence interval (CI) for the group difference (MMRV Group minus MMR+V Group) in seroconversion rate for anti-rubella was above -10%.

Comparison groups	MMRV Group v MMR+V Group
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Number of subjects included in analysis	457
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05 ^[3]
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:

[3] - The p-values for all reactogenicity comparisons were calculated using a two-sided Fisher Exact test.

Statistical analysis title	Non-inferiority - vaccine response to anti-VZV
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Statistical analysis description:

Non-inferiority of MMRV vaccine vs MMR and V administered as concomitant vaccine 42-56 days after vaccination at Day 0 in terms of of anti-varicella zoster virus (VZV) seroconversion rates. Non-inferiority with respect to seroconversion rates for VZV 42-56 days after vaccination was concluded if the lower limit of the two-sided standardized asymptotic 95% confidence interval (CI) for the group difference (MMRV Group minus MMR+V Group) in seroconversion rate for anti-VZV was above -10%.

Comparison groups	MMRV Group v MMR+V Group
Number of subjects included in analysis	457
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.05 ^[4]
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:

[4] - The p-values for all reactogenicity comparisons were calculated using a two-sided Fisher Exact test.

Secondary: Antibody concentrations against measles.

End point title	Antibody concentrations against measles.
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End point description:

Antibody titers were summarized by Geometric Mean Concentrations (GMCs) with their 95% CIs.

End point type	Secondary
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End point timeframe:

At 42-days after vaccination.

End point values	MMRV Group	MMR+V 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 titers were summarized by Geometric Mean Concentrations (GMCs) with their 95% CIs.
End point type	Secondary
End point timeframe:	At 42-days after vaccination.

End point values	MMRV Group	MMR+V 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 titers were summarized by Geometric Mean Concentrations (GMCs) with their 95% CIs.
End point type	Secondary
End point timeframe:	At 42-days after vaccination.

End point values	MMRV Group	MMR+V 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 varicela viruses.

End point title	Antibody titers against varicela viruses.
End point description:	Antibody titers were summarized by Geometric Mean Titers (GMTs) with their 95% CIs.
End point type	Secondary
End point timeframe:	At 42-days after vaccination.

End point values	MMRV Group	MMR+V 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:	
Within 4-days (Days 0-3) post-vaccination period.	

End point values	MMRV Group	MMR+V 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.
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End point description:

Solicited general symptoms assessed were fever (defined as rectal temperature $\geq 38^{\circ}\text{C}$), rash, meningism and parotid gland swelling. Any was defined as incidence of the specified symptoms regardless of intensity or relationship to study vaccine. Grade 3 rash was defined as more than 150 lesions. Grade 3 fever was defined as fever (rectal temperature) $> 39.5^{\circ}\text{C}$. Grade 3 meningism and parotid gland swelling was defined as 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	MMRV Group	MMR+V 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	MMRV Group	MMR+V 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:

From the study dose until study end (Day 0 to Day 43-57).

End point values	MMRV Group	MMR+V 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:

Serious Adverse Events: entire study period (Day 0 to Day 43-57); Solicited local: During the 4-day (Days 0-3) post vaccination period; Unsolicited symptoms and solicited general symptoms: Within 43 day post vaccination period.

Adverse event reporting additional description:

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	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	13.0
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Reporting groups

Reporting group title	MMRV Group
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Reporting group description: -

Reporting group title	MMR+V Group
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Reporting group description: -

Serious adverse events	MMRV Group	MMR+V 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	MMRV Group	MMR+V Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	202 / 313 (64.54%)	88 / 161 (54.66%)	
General disorders and administration site conditions			
Pain			
alternative assessment type: Systematic			

subjects affected / exposed ^[1]	15 / 310 (4.84%)	10 / 159 (6.29%)	
occurrences (all)	15	10	
Redness			
alternative assessment type: Systematic			
subjects affected / exposed ^[2]	26 / 310 (8.39%)	21 / 159 (13.21%)	
occurrences (all)	26	21	
Fever			
alternative assessment type: Systematic			
subjects affected / exposed ^[3]	202 / 310 (65.16%)	82 / 159 (51.57%)	
occurrences (all)	202	82	
Rash			
alternative assessment type: Systematic			
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