



Clinical trial results:

Open, multicenter, randomized, controlled phase IIIb study evaluating the immunogenicity and safety of subcutaneous versus intramuscular administration of GlaxoSmithKline Biologicals' combined measles mumps rubella varicella vaccine (MeMuRu-OKA) to healthy children aged 11 to 21 months

Summary

EudraCT number	2005-005944-22
Trial protocol	DE
Global end of trial date	13 December 2006

Results information

Result version number	v1 (current)
This version publication date	10 July 2019
First version publication date	10 July 2019

Trial information

Trial identification

Sponsor protocol code	106670
-----------------------	--------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00351923
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 Disclosure Advisor, GlaxoSmithKline Biologicals, +(44) 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Disclosure Advisor, GlaxoSmithKline Biologicals, +(44) 2089904466, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	07 February 2008
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 December 2006
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary Objective: 1. To evaluate geometric mean titer (GMT) and seroconversion rate to varicella zoster virus (VZV) after intramuscular (IM) and subcutaneous (SC) injection of GlaxoSmithKline Biologicals' (GSK's) combined measles-mumps-rubella-varicella (MeMuRu-OKA) vaccine. Secondary Objectives: 1. To evaluate the cell-mediated immunity (CMI) to varicella and measles after IM and SC injection of GSK's MeMuRu-OKA vaccine. 2. To quantify the immediate vaccination pain after IM and SC injection of GSK's MeMuRu-OKA vaccine. 3. To evaluate GMT and seroconversion rate to measles, mumps, and rubella, after IM and SC injection of GSK's MeMuRu-OKA vaccine. 4. To evaluate incidence, nature and severity of local, general, and serious adverse events after IM and SC injection of GSK's MeMuRu-OKA vaccine.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 March 2006
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	Germany: 328
Worldwide total number of subjects	328
EEA total number of subjects	328

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)	328
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:

Out of 328 subjects enrolled in the study, only 318 completed the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	IM Group

Arm description:

Healthy male and female subjects aged between 11 and 21 months at the time of first vaccination, who received 2 doses of GlaxoSmithKline Biologicals' combined measles mumps rubella varicella (MMRV) vaccine by intramuscular (IM) injection in the deltoid region of the left arm at Day 0 and Week 6.

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	Intramuscular use

Dosage and administration details:

Subjects in the IM Group were administered 2 doses of the vaccine intramuscularly in the deltoid region of the left arm at Day 0 and Week 6.

Arm title	SC Group
------------------	----------

Arm description:

Healthy male and female subjects aged between 11 and 21 months at the time of first vaccination, who received 2 doses of GlaxoSmithKline Biologicals' combined measles mumps rubella varicella (MMRV) vaccine by subcutaneous (SC) injection in the deltoid region of the left arm at Day 0 and Week 6.

Arm type	Active comparator
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:

Subjects in the SC Group were administered 2 doses of the vaccine subcutaneously in the deltoid region of the left arm at Day 0 and Week 6.

Number of subjects in period 1	IM Group	SC Group
Started	166	162
Completed	161	157
Not completed	5	5
Consent withdrawn by subject	1	1
Lack of interest in participation	1	-
Unwilling to continue in study	-	1
Lost to follow-up	3	1
Non-serious Adverse Event	-	1
Protocol deviation	-	1

Baseline characteristics

Reporting groups

Reporting group title	IM Group
-----------------------	----------

Reporting group description:

Healthy male and female subjects aged between 11 and 21 months at the time of first vaccination, who received 2 doses of GlaxoSmithKline Biologicals' combined measles mumps rubella varicella (MMRV) vaccine by intramuscular (IM) injection in the deltoid region of the left arm at Day 0 and Week 6.

Reporting group title	SC Group
-----------------------	----------

Reporting group description:

Healthy male and female subjects aged between 11 and 21 months at the time of first vaccination, who received 2 doses of GlaxoSmithKline Biologicals' combined measles mumps rubella varicella (MMRV) vaccine by subcutaneous (SC) injection in the deltoid region of the left arm at Day 0 and Week 6.

Reporting group values	IM Group	SC Group	Total
Number of subjects	166	162	328
Age categorical			
Months			
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)	166	162	328
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	12.7	12.5	
standard deviation	± 2.2	± 2.0	-
Gender categorical			
Units: Subjects			
Female	86	72	158
Male	80	90	170

End points

End points reporting groups

Reporting group title	IM Group
Reporting group description: Healthy male and female subjects aged between 11 and 21 months at the time of first vaccination, who received 2 doses of GlaxoSmithKline Biologicals' combined measles mumps rubella varicella (MMRV) vaccine by intramuscular (IM) injection in the deltoid region of the left arm at Day 0 and Week 6.	
Reporting group title	SC Group
Reporting group description: Healthy male and female subjects aged between 11 and 21 months at the time of first vaccination, who received 2 doses of GlaxoSmithKline Biologicals' combined measles mumps rubella varicella (MMRV) vaccine by subcutaneous (SC) injection in the deltoid region of the left arm at Day 0 and Week 6.	

Primary: Percentage of seroconverted subjects with varicella zoster virus (VZV) antibody titer above or below cut-off value

End point title	Percentage of seroconverted subjects with varicella zoster virus (VZV) antibody titer above or below cut-off value
End point description: Seroconversion was defined as the appearance of antibodies [i.e., antibody titre greater than or equal to (\geq) the cut-off value of 1:4] in the serum of subjects seronegative before vaccination. A seronegative subject was one without detectable serum antibodies.	
End point type	Primary
End point timeframe: At Week 12 (i.e. 42-56 days after administration of 2nd vaccine dose at Week 6)	

End point values	IM Group	SC Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	130		
Units: Percentage of subjects				
number (confidence interval 95%)				
Percentage of subjects	100.0 (97.2 to 100.0)	100.0 (97.2 to 100.0)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: Non-inferiority of IM Group as compared to SC Group in terms of the difference in the percentage of subjects with anti-varicella titer above the specified cut off with its two-sided 95% CI in initially seronegative subjects.	
Comparison groups	IM Group v SC Group

Number of subjects included in analysis	258
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[1]
Parameter estimate	Difference in seroconversion rate (%)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.1
upper limit	5.04

Notes:

[1] - Lower limit of the two-sided 95% CI for group difference in seroconversion rates for antibodies to varicella virus 42-56 days after the second dose between the IM Group and the SC Group (IM Group minus SC Group) should be equal to or above -5% (clinical limit for non-inferiority).

Secondary: Anti-VZV antibody titers

End point title	Anti-VZV antibody titers
End point description:	Antibody titer against VZV was determined by Immunofluorescence assay (IFA) and expressed as geometric mean titers (GMTs).
End point type	Secondary
End point timeframe:	At Week 12 (i.e. 42-56 days after administration of 2nd vaccine dose at Week 6)

End point values	IM Group	SC Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	128	130		
Units: Titers				
geometric mean (confidence interval 95%)				
Titers	3388.8 (2768.3 to 4148.4)	2575.7 (2081.5 to 3187.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of varicella-specific Cluster of Differentiation 4 (CD4+) and CD8+ T-cell responses

End point title	Frequency of varicella-specific Cluster of Differentiation 4 (CD4+) and CD8+ T-cell responses
End point description:	Varicella-specific CD4+/CD8+ T-cells frequency was assessed by Flow cytometry in ex vivo stimulated peripheral blood mononuclear cells (PBMC) and expressed as positive cells per 10 ⁶ PBMC. Tested cytokines were CD40 ligand (CD40L), interferon gamma (IFN γ), interleukin-2 (IL-2) and tumor necrosis factor alpha (TNF α).
End point type	Secondary

End point timeframe:

At Week 12 (i.e. 42-56 days after administration of 2nd vaccine dose at Week 6)

End point values	IM Group	SC Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	26		
Units: Cells/10 ⁶ PBMC				
arithmetic mean (standard deviation)				
Varicella-specific CD4-CD40L	3.02 (± 2.07)	1.95 (± 2.40)		
Varicella-specific CD4-IFN γ	3.52 (± 1.76)	3.19 (± 1.90)		
Varicella-specific CD4-IL-2	3.31 (± 2.20)	1.88 (± 2.68)		
Varicella-specific CD4-TNF α	3.08 (± 2.17)	2.49 (± 2.51)		
Varicella-specific CD4-All Doubles	3.45 (± 2.13)	2.47 (± 2.30)		
Varicella-specific CD8-CD40L	0.56 (± 2.29)	0.16 (± 1.37)		
Varicella-specific CD8-IFN γ	0.68 (± 2.10)	0.16 (± 1.31)		
Varicella-specific CD8-IL-2	0.58 (± 2.64)	-0.02 (± 2.46)		
Varicella-specific CD8-TNF α	0.52 (± 2.54)	-0.14 (± 2.54)		
Varicella-specific CD8-All Doubles	0.61 (± 2.66)	0.01 (± 2.43)		

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of measles-specific CD4+ and CD8+ T-cell responses

End point title	Frequency of measles-specific CD4+ and CD8+ T-cell responses
-----------------	--

End point description:

Measles-specific CD4+/CD8+ T-cells frequency was assessed by Flow cytometry in ex vivo stimulated PBMC and expressed as positive cells per 10⁶ PBMC. Tested cytokines were CD40 ligand (CD40L), interferon gamma (IFN γ), interleukin-2 (IL-2) and tumor necrosis factor alpha (TNF α).

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

End point timeframe:

At Week 12 (i.e. 42-56 days after administration of 2nd vaccine dose at Week 6)

End point values	IM Group	SC Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	24		
Units: Cells/10 ⁶ PBMC				
arithmetic mean (standard deviation)				
Measles-specific CD4-CD40L	0.91 (± 2.35)	0.29 (± 2.55)		
Measles-specific CD4-IFN γ	-0.05 (± 1.80)	-0.19 (± 1.77)		
Measles-specific CD4-IL-2	0.11 (± 2.30)	0.35 (± 2.79)		
Measles-specific CD4-TNF α	0.88 (± 2.16)	0.77 (± 2.65)		
Measles-specific CD4-All Doubles	1.14 (± 2.27)	0.45 (± 2.80)		

Measles-specific CD8-CD40L	0.04 (± 1.09)	0 (± 1.08)		
Measles-specific CD8-IFN γ	0.25 (± 1.33)	-0.30 (± 1.24)		
Measles-specific CD8-IL-2	-0.41 (± 2.33)	-0.52 (± 2.39)		
Measles-specific CD8-TNF α	-0.35 (± 2.40)	-0.99 (± 2.42)		
Measles-specific CD8-All Doubles	-0.35 (± 2.40)	-0.66 (± 2.19)		

Statistical analyses

No statistical analyses for this end point

Secondary: Frequency of mumps-specific CD4+ and CD8+ T-cell responses

End point title	Frequency of mumps-specific CD4+ and CD8+ T-cell responses
-----------------	--

End point description:

Mumps-specific CD4+/CD8+ T-cells frequency was assessed by Flow cytometry in ex vivo stimulated PBMC and expressed as positive cells per 10⁶ PBMC. Tested cytokines were CD40 ligand (CD40L), interferon gamma (IFN γ), interleukin-2 (IL-2) and tumor necrosis factor alpha (TNF α).

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

End point timeframe:

At Week 12 (i.e. 42-56 days after administration of 2nd vaccine dose at Week 6)

End point values	IM Group	SC Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	25		
Units: Cells/10 ⁶ PBMC				
arithmetic mean (standard deviation)				
Mumps-specific CD4-CD40L	1.54 (± 2.04)	1.74 (± 2.05)		
Mumps-specific CD4-IFN γ	2.24 (± 2.06)	2.49 (± 1.76)		
Mumps-specific CD4-IL-2	1.91 (± 2.57)	1.39 (± 2.37)		
Mumps-specific CD4-TNF α	2.22 (± 1.78)	1.99 (± 2.08)		
Mumps-specific CD4-All Doubles	2.11 (± 2.18)	1.68 (± 2.36)		
Mumps-specific CD8-CD40L	0.26 (± 1.68)	0.19 (± 1.37)		
Mumps-specific CD8-IFN γ	-0.25 (± 0.97)	0.18 (± 1.37)		
Mumps-specific CD8-IL-2	0.52 (± 2.19)	-0.70 (± 2.32)		
Mumps-specific CD8-TNF α	0.46 (± 2.16)	-0.18 (± 2.62)		
Mumps-specific CD8-All Doubles	0.28 (± 2.21)	-0.15 (± 2.67)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of seroconverted subjects anti-measles, anti-mumps and anti-rubella antibody titers above or below cut-off value

End point title	Percentage of seroconverted subjects anti-measles, anti-mumps and anti-rubella antibody titers above or below cut-off value
-----------------	---

End point description:

Seroconversion was defined as the appearance of antibodies [i.e., antibody titre \geq the cut-off value] in the serum of subjects seronegative before vaccination. A seronegative subject was one without detectable serum antibodies.

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

End point timeframe:

At Week 12 (i.e. 42-56 days after administration of 2nd vaccine dose at Week 6)

End point values	IM Group	SC Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	140	140		
Units: Percentage of subjects				
number (confidence interval 95%)				
Anti-measles antibody \geq 150 mIU/mL	99.3 (96.0 to 100.0)	98.6 (94.9 to 99.8)		
Anti-mumps antibody \geq 231 U/mL	100.0 (97.4 to 100.0)	99.3 (96.1 to 100.0)		
Anti-rubella antibody \geq 4 IU/mL	100.0 (97.4 to 100.0)	100.0 (97.4 to 100.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-measles, anti-mumps and anti-rubella antibody titers

End point title	Anti-measles, anti-mumps and anti-rubella antibody titers
-----------------	---

End point description:

Antibody concentrations against measles, mumps and rubella were determined by Enzyme Linked Immunosorbent Assay (ELISA) and expressed as GMTs.

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

End point timeframe:

At Week 12 (i.e. 42-56 days after administration of 2nd vaccine dose at Week 6)

End point values	IM Group	SC Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	140	140		
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-measles	4451.3 (3843.6 to 5155.1)	4183.8 (3618.2 to 4837.8)		
Anti-mumps	2298.1 (2064.4 to 2558.1)	2194.8 (1967.7 to 2448.2)		

Anti-rubella	93.1 (83.5 to 103.7)	106.3 (95.4 to 118.6)		
--------------	----------------------	-----------------------	--	--

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with immediate vaccination pain assessed by scores on the Visual Analogue Scale (VAS)

End point title	Number of subjects with immediate vaccination pain assessed by scores on the Visual Analogue Scale (VAS)
-----------------	--

End point description:

Immediate vaccination pain was recorded by the investigator who administered the vaccine, immediately before each vaccination, on the VAS. Scores ranged from 1 (no pain) to 5 (worst pain).

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

End point timeframe:

Immediately before vaccination (i.e. at Day 0 and Week 6)

End point values	IM Group	SC Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	166	162		
Units: Participants				
Score 1, Dose 1	72	81		
Score 2, Dose 1	56	49		
Score 3, Dose 1	26	19		
Score 4, Dose 1	7	7		
Score 5, Dose 1	5	6		
Score 1, Dose 2 (N=161; 161)	89	89		
Score 2, Dose 2 (N=161; 161)	49	50		
Score 3, Dose 2 (N=161; 161)	20	16		
Score 4, Dose 2 (N=161; 161)	0	5		
Score 5, Dose 2 (N=161; 161)	3	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with immediate vaccination pain assessed by scores on the VAS

End point title	Number of subjects with immediate vaccination pain assessed by scores on the VAS
-----------------	--

End point description:

Immediate vaccination pain was recorded by the investigator who administered the vaccine, within 30 seconds after each vaccination, on the VAS. Scores ranged from 1 (no pain) to 5 (worst pain).

End point type	Secondary
End point timeframe:	
30 seconds after each vaccination (i.e. at Day 0 and Week 6)	

End point values	IM Group	SC Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	166	162		
Units: Participants				
Score 1, Dose 1	16	23		
Score 2, Dose 1	39	38		
Score 3, Dose 1	44	37		
Score 4, Dose 1	34	34		
Score 5, Dose 1	33	30		
Score 1, Dose 2 (N=161; 161)	27	33		
Score 2, Dose 2 (N=161; 161)	42	45		
Score 3, Dose 2 (N=161; 161)	48	33		
Score 4, Dose 2 (N=161; 161)	21	23		
Score 5, Dose 2 (N=161; 161)	23	27		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and grade 3 solicited local adverse events (AEs)

End point title	Number of subjects with any and grade 3 solicited local adverse events (AEs)
End point description:	
Assessed solicited local AEs included pain, redness and swelling at the injection site. Any = any solicited local AE irrespective of its intensity grade. Grade 3 pain = cried when limb was moved/spontaneously painful. Grade 3 redness, swelling = affected area was >20 mm in diameter.	
End point type	Secondary
End point timeframe:	
During the 4-day follow-up period after each vaccination	

End point values	IM Group	SC Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	166	162		
Units: Participants				
Any Pain, Dose 1	14	14		
Grade 3 Pain, Dose 1	0	0		
Any Redness, Dose 1	40	50		
Grade 3 Redness, Dose 1	1	1		
Any Swelling, Dose 1	10	18		

Grade 3 Swelling, Dose 1	1	0		
Any Pain, Dose 2 (N=161; 161)	15	8		
Grade 3 Pain, Dose 2 (N=161; 161)	0	0		
Any Redness, Dose 2 (N=161; 161)	45	39		
Grade 3 Redness, Dose 2 (N=161; 161)	0	2		
Any Swelling, Dose 2 (N=161; 161)	15	20		
Grade 3 Swelling, Dose 2 (N=161; 161)	1	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any, grade 3 and vaccine-related solicited general AEs

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

End point description:

Assessed solicited general AEs were fever, rash, parotid/salivary gland swelling and signs of meningism including febrile convulsions. Any = any solicited general AE irrespective of its intensity grade and relationship to vaccination. Any fever = any rectal temperature $\geq 38.0^{\circ}\text{C}$. Grade 3 fever = rectal temperature $> 39.5^{\circ}\text{C}$. Any rash = any kind of skin eruption. Grade 3 rash = > 150 lesions. Grade 3 parotitis = swelling with accompanying general symptoms. Grade 3 febrile convulsions/meningism = febrile convulsions/meningism that prevented normal everyday activities. Related = AE considered by the investigator to have a causal relationship to vaccination.

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

End point timeframe:

During the 43-day follow-up period after each vaccination

End point values	IM Group	SC Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	166	162		
Units: Participants				
Any Fever (Rectally), Dose 1	121	114		
Grade 3 Fever (Rectally), Dose 1	20	25		
Related Fever (Rectally), Dose 1	76	69		
Any Rash, Dose 1	43	33		
Grade 3 Rash, Dose 1	6	5		
Related Rash, Dose 1	10	11		
Any Parotitis, Dose 1	0	0		
Grade 3 Parotitis, Dose 1	0	0		
Related Parotitis, Dose 1	0	0		
Any Febrile Convulsions, Dose 1	1	0		
Grade 3 Febrile Convulsions, Dose 1	0	0		
Related Febrile Convulsions, Dose 1	0	0		
Any Fever (Rectally), Dose 2 (N=161; 161)	67	68		
Grade 3 Fever (Rectally), Dose 2 (N=161; 161)	12	12		

Related Fever (Rectally), Dose 2 (N=161; 161)	26	20		
Any Rash, Dose 2 (N=161; 161)	25	20		
Grade 3 Rash, Dose 2 (N=161; 161)	3	1		
Related Rash, Dose 2 (N=161; 161)	4	1		
Any Parotitis, Dose 2 (N=161; 161)	0	0		
Grade 3 Parotitis, Dose 2 (N=161; 161)	0	0		
Related Parotitis, Dose 2 (N=161; 161)	0	0		
Any Febrile Convulsions, Dose 2 (N=161; 161)	1	0		
Grade 3 Febrile Convulsions, Dose 2 (N=161; 161)	0	0		
Related Febrile Convulsions, Dose 2 (N=161; 161)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any, grade 3 and vaccine-related unsolicited AEs

End point title	Number of subjects with any, grade 3 and vaccine-related unsolicited AEs
-----------------	--

End point description:

An unsolicited AE was any AE reported in addition to those solicited during the clinical study. Also, any "solicited" AE with onset outside the specified period of follow-up for solicited AEs was reported as an unsolicited AE. Any = any unsolicited AE irrespective of its intensity grade and relationship to vaccination. Grade 3 AE = AE that prevented normal activity. Related AE = AE considered by the investigator to be causally related to the study vaccination.

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

End point timeframe:

During the 43-day follow-up period after each vaccination

End point values	IM Group	SC Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	166	162		
Units: Participants				
Any AE, Dose 1	79	82		
Grade 3 AE, Dose 1	7	5		
Related AE, Dose 1	6	9		
Any AE, Dose 2 (N=161; 161)	62	62		
Grade 3 AE, Dose 2 (N=161; 161)	6	3		
Related AE, Dose 2 (N=161; 161)	3	3		

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects with any serious adverse events (SAEs)
-----------------	---

End point description:

SAE was defined as any untoward medical occurrence that resulted in death, was life-threatening, resulted in persistent or significant disability/incapacity, required in-patient hospitalization or prolongation of existing hospitalization or was a congenital anomaly/birth defect in the offspring of a study subject. Any = any SAE irrespective of its intensity grade and relationship to vaccination.

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

End point timeframe:

Throughout the entire study period (Day 0 up to Week 12)

End point values	IM Group	SC Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	166	162		
Units: Participants				
Participants	8	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited local AEs: During the 4-day follow-up period after each vaccination; Solicited general AEs and unsolicited AEs: During the 43-day follow-up period after each vaccination; SAEs: During the entire study period (Day 0 up to Week 12).

Adverse event reporting additional description:

Total Number (#) of Participants Affected by Other (non-serious) AEs was analyzed separately for expected & unexpected AEs. Performing consolidated analysis was not technically possible & the relevant data is no longer available. Total #Participants Affected in Other AEs Table is currently populated by the highest value of #Participants affected.

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

Dictionary used

Dictionary name	MedDRA
-----------------	--------

Dictionary version	10.1
--------------------	------

Reporting groups

Reporting group title	IM Group
-----------------------	----------

Reporting group description:

Healthy male and female subjects aged between 11 and 21 months at the time of first vaccination, who received 2 doses of MMRV vaccine by intramuscular (IM) injection in the deltoid region of the left arm at Day 0 and Week 6.

Reporting group title	SC Group
-----------------------	----------

Reporting group description:

Healthy male and female subjects aged between 11 and 21 months at the time of first vaccination, who received 2 doses of MMRV vaccine by subcutaneous (SC) injection in the deltoid region of the left arm at Day 0 and Week 6.

Serious adverse events	IM Group	SC Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	8 / 166 (4.82%)	1 / 162 (0.62%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Nervous system disorders			
Febrile Convulsion			
subjects affected / exposed	2 / 166 (1.20%)	0 / 162 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ataxia			
subjects affected / exposed	0 / 166 (0.00%)	1 / 162 (0.62%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Somnolence			

subjects affected / exposed	0 / 166 (0.00%)	1 / 162 (0.62%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	3 / 166 (1.81%)	0 / 162 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis rotavirus			
subjects affected / exposed	2 / 166 (1.20%)	0 / 162 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 166 (0.60%)	0 / 162 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngotonsillitis			
subjects affected / exposed	1 / 166 (0.60%)	0 / 162 (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			
Anorexia			
subjects affected / exposed	1 / 166 (0.60%)	0 / 162 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	IM Group	SC Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	121 / 166 (72.89%)	114 / 162 (70.37%)	
General disorders and administration site conditions			
Pain, Dose 1	Additional description: Solicited local AE reported during the 4-day post-vaccination period after Dose 1		

subjects affected / exposed occurrences (all)	14 / 166 (8.43%) 14	14 / 162 (8.64%) 14	
Pain, Dose 2	Additional description: Solicited local AE reported during the 4-day post-vaccination period after Dose 2		
subjects affected / exposed ^[1] occurrences (all)	15 / 161 (9.32%) 15	8 / 161 (4.97%) 8	
Redness, Dose 1	Additional description: Solicited local AE reported during the 4-day post-vaccination period after Dose 1		
subjects affected / exposed occurrences (all)	40 / 166 (24.10%) 40	50 / 162 (30.86%) 50	
Redness, Dose 2	Additional description: Solicited local AE reported during the 4-day post-vaccination period after Dose 2		
subjects affected / exposed ^[2] occurrences (all)	45 / 161 (27.95%) 45	39 / 161 (24.22%) 39	
Swelling, Dose 1	Additional description: Solicited local AE reported during the 4-day post-vaccination period after Dose 1		
subjects affected / exposed occurrences (all)	10 / 166 (6.02%) 10	18 / 162 (11.11%) 18	
Swelling, Dose 2	Additional description: Solicited local AE reported during the 4-day post-vaccination period after Dose 2		
subjects affected / exposed ^[3] occurrences (all)	15 / 161 (9.32%) 15	20 / 161 (12.42%) 20	
Fever, Dose 1	Additional description: Solicited general AE reported during the 43-day post-vaccination period after Dose 1		
subjects affected / exposed occurrences (all)	121 / 166 (72.89%) 121	114 / 162 (70.37%) 114	
Fever, Dose 2	Additional description: Solicited general AE reported during the 43-day post-vaccination period after Dose 2		
subjects affected / exposed ^[4] occurrences (all)	67 / 161 (41.61%) 67	68 / 161 (42.24%) 68	
Rash, Dose 1	Additional description: Solicited general AE reported during the 43-day post-vaccination period after Dose 1		
subjects affected / exposed occurrences (all)	43 / 166 (25.90%) 43	33 / 162 (20.37%) 33	
Rash, Dose 2	Additional description: Solicited general AE reported during the 43-day post-vaccination period after Dose 2		
subjects affected / exposed ^[5] occurrences (all)	25 / 161 (15.53%) 25	20 / 161 (12.42%) 20	
Gastrointestinal disorders			
Teething, Dose 1	Additional description: Unsolicited AE reported during the 43-day post-vaccination period after Dose 1		
subjects affected / exposed occurrences (all)	9 / 166 (5.42%) 9	2 / 162 (1.23%) 2	

Enteritis, Dose 1 subjects affected / exposed occurrences (all)	Additional description: Unsolicited AE reported during the 43-day post-vaccination period after Dose 1		
	3 / 166 (1.81%)	9 / 162 (5.56%)	
	3	9	
Infections and infestations Upper Respiratory Tract Infection, Dose 1 subjects affected / exposed occurrences (all)	Additional description: Unsolicited AE reported during the 43-day post-vaccination period after Dose 1		
	13 / 166 (7.83%)	12 / 162 (7.41%)	
Upper Respiratory Tract Infection, Dose 2 subjects affected / exposed ^[6] occurrences (all)	Additional description: Unsolicited AE reported during the 43-day post-vaccination period after Dose 2		
	10 / 161 (6.21%)	12 / 161 (7.45%)	
Otitis Media, Dose 1 subjects affected / exposed occurrences (all)	Additional description: Unsolicited AE reported during the 43-day post-vaccination period after Dose 1		
	7 / 166 (4.22%)	9 / 162 (5.56%)	
Gastroenteritis, Dose 1 subjects affected / exposed occurrences (all)	Additional description: Unsolicited AE reported during the 43-day post-vaccination period after Dose 1		
	7 / 166 (4.22%)	9 / 162 (5.56%)	
Rhinitis, Dose 2 subjects affected / exposed ^[7] occurrences (all)	Additional description: Unsolicited AE reported during the 43-day post-vaccination period after Dose 2		
	9 / 161 (5.59%)	10 / 161 (6.21%)	

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: Assessment for this event was done in subjects with available results.

[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: Assessment for this event was done in subjects with available results.

[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: Assessment for this event was done in subjects with available results.

[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: Assessment for this event was done in subjects with available results.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Assessment for this event was done in subjects with available results.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Assessment for this event was done in subjects with available results.

[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.

Justification: Assessment for this event was done in subjects with available results.

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