Clinical trial results:
A phase IIIB, partially blind, randomized study to evaluate the immunogenicity and safety of GlaxoSmithKline Biologicals' measles-mumps-rubella-varicella vaccine (MeMuRu-OKA) given to healthy children during the second year of life following a 4-week and a 12-month interval between two doses

Summary

EudraCT number	2004-004371-11
Trial protocol	DE BE
Global end of trial date	23 May 2007

Results information

Result version number	v1 (current)
This version publication date	23 May 2016
First version publication date	07 June 2015

Trial information

Trial identification

Sponsor protocol code	103388 & 104690

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00127010
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	23 May 2007
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 May 2007
Global end of trial reached?	Yes
Global end of trial date	23 May 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the immunogenicity of a 4-week interval and a 12-month interval between two doses of MeMuRu-OKA 42-56 days after the second dose for all antigens.

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 the administration of vaccines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 November 2005
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	Belgium: 44
Country: Number of subjects enrolled	Germany: 386
Country: Number of subjects enrolled	Netherlands: 130
Worldwide total number of subjects	560
EEA total number of subjects	560

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)	560
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:

One subject from the total number of 560 subjects had a subject number allocated but no study vaccine administered and therefore not included in "Started".

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 Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Single blind
Roles blinded	Subject

Blinding implementation details:

The study was open with respect to the 2 groups randomized to a 4-week interval schedule versus the group with a 12-month interval schedule and single-blind with respect to the group randomized to a 4-week interval schedule of MMRV versus group receiving MMR up to Week 10, when they were offered licensed varicella vaccine, to be administered outside of the study.

Arms

Are arms mutually exclusive?	Yes
Arm title	MMRV/4W Group

Arm description:

Subjects received two doses of MMRV vaccine 4 weeks apart (Day 0 and Week 4).

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

Dosage and administration details:

Two doses of Priorix™-Tetra vaccine (MMRV) 4 weeks apart (Day 0 and Week 4) administered subcutaneously in the left deltoid region.

Arm title	MMRV/12M Group

Arm description:

Subjects received two doses of Priorix™-Tetra vaccine (MMRV) 12 months apart (Day 0 and Month 12).

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

Dosage and administration details:

Two doses of Priorix™-Tetra vaccine (MMRV) 12 months apart (Day 0 and Month 12) administered subcutaneously in the left deltoid region.

Arm title	MMR Group

Arm description:

Subjects received two doses of Priorix™ vaccine (MMR) 4 weeks apart (Day 0 and Week 4)

Arm type	Active comparator
Investigational medicinal product name	Priorix™
Investigational medicinal product code	MeMuRu
Other name	
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Intramuscular use, Subcutaneous use

Dosage and administration details:

Two doses of Priorix™ vaccine (MMR) 4 weeks apart (Day 0 and Week 4) administered subcutaneously in the left deltoid region.

Number of subjects in period 1[1]	MMRV/4W Group	MMRV/12M Group	MMR Group
Started	188	184	187
Completed	181	180	184
Not completed	7	4	3
Adverse event, serious fatal	-	-	1
Consent withdrawn by subject	5	2	1
Adverse event, non-fatal	1	-	-
Lost to follow-up	1	2	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: One subject from the total number of 560 subjects had a subject number allocated but no study vaccine administered and therefore not included in "Started".

Baseline characteristics

Reporting groups	
Reporting group title	MMRV/4W Group
Reporting group description:	
Subjects received two doses of MMRV vaccine 4 weeks apart (Day 0 and Week 4).	
Reporting group title	MMRV/12M Group
Reporting group description:	
Subjects received two doses of Priorix™-Tetra vaccine (MMRV) 12 months apart (Day 0 and Month 12).	
Reporting group title	MMR Group
Reporting group description:	
Subjects received two doses of Priorix™ vaccine (MMR) 4 weeks apart (Day 0 and Week 4)	

Reporting group values	MMRV/4W Group	MMRV/12M Group	MMR Group
Number of subjects	188	184	187
Age categorical Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous Units: months			
arithmetic mean	12	12	12.1
standard deviation	± 0.83	± 0.84	± 0.9
Gender categorical Units: Subjects			
Female	92	96	92
Male	96	88	95

Reporting group values	Total		
Number of subjects	559		
Age categorical Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	0		

From 65-84 years	0		
85 years and over	0		

Age continuous Units: months arithmetic mean standard deviation	- 		
Gender categorical Units: Subjects			
Female	280		
Male	279		

End points

End points reporting groups

Reporting group title	MMRV/4W Group
Reporting group description:	
Subjects received two doses of MMRV vaccine 4 weeks apart (Day 0 and Week 4).	
Reporting group title	MMRV/12M Group
Reporting group description:	
Subjects received two doses of Priorix™-Tetra vaccine (MMRV) 12 months apart (Day 0 and Month 12).	
Reporting group title	MMR Group
Reporting group description:	
Subjects received two doses of Priorix™ vaccine (MMR) 4 weeks apart (Day 0 and Week 4)	

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

End point title	Number of subjects seroconverted for measles, mumps, rubella and varicella antibodies above the cut-off value.[1][2]

End point description:

Seroconversion was defined as the appearance of antibodies (i.e. titer greater than or equal to the cut-off value) in the serum of subjects seronegative before vaccination. The cut-off values for seroconversion was 150 mIU/mL, 231 U/mL, 4 IU/mL and 1:4 dilution for measles, mumps, rubella and varicella, respectively. This outcome measure concerns the MMRV/4W Group and MMRV/12M Group.

End point type	Primary

End point timeframe:

Approximately 42-56 days after the second dose of MMRV vaccine (Week 10 for the MMRV/4W Groups and Month 13.5 for the MMRV/12M Group).

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.
[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This outcome measure concerns the MMRV/4W Group and MMRV/12M Group.

End point values	MMRV/4W Group	MMRV/12M Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	110	137		
Units: Subjects				
anti-measles ≥ 150 mIU/mL	108	124		
anti-mumps ≥ 231 U/ML	105	124		
anti-rubella ≥ 4 IU/mL	110	124		
IgG varicella antibodies ≥ 1:4 dilution	101	116		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroconverted for measles, mumps, rubella and varicella antibodies above the cut-off value.

End point title	Number of subjects seroconverted for measles, mumps, rubella and varicella antibodies above the cut-off value.[3]

End point description:

Seroconversion was defined as the appearance of antibodies (i.e. titer greater than or equal to the cut-off value) in the serum of subjects seronegative before vaccination. The cut-off values for seroconversion was 150 mIU/mL, 231 U/mL, 4 IU/mL and 1:4 dilution for measles, mumps, rubella and varicella, respectively. This outcome measure concerns the MMRV/12M Group only.

End point type	Secondary

End point timeframe:

At 42-56 days after the first dose of MMRV vaccine.

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This outcome measure concerns the MMRV/12M Group only.

End point values	MMRV/12M Group			
Subject group type	Reporting group			
Number of subjects analysed	137			
Units: Subjects				
anti-measles ≥ 150 mIU/mL	134			
anti-mumps ≥ 231 U/ML	125			
anti-rubella ≥ 4 IU/mL	133			
IgG varicella antibodies ≥ 1:4 dilution	127			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroconverted for measles, mumps, rubella and varicella antibodies above the cut-off value.

End point title	Number of subjects seroconverted for measles, mumps, rubella and varicella antibodies above the cut-off value.[4]

End point description:

Seroconversion was defined as the appearance of antibodies (i.e. titer greater than or equal to the cut-off value) in the serum of subjects seronegative before vaccination. The cut-off values for seroconversion was 150 mIU/mL, 231 U/mL, 4 IU/mL and 1:4 dilution for measles, mumps, rubella and varicella, respectively. This outcome measure concerns the MMRV/4W Group only.

End point type	Secondary

End point timeframe:

At 28-30 days after the first dose of MMRV vaccine.

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This outcome measure concerns the MMRV/4W Group only.

End point values	MMRV/4W Group			
Subject group type	Reporting group			
Number of subjects analysed	110			
Units: Subjects				
anti-measles ≥ 150 mIU/mL	108			
anti-mumps ≥ 231 U/ML	78			
anti-rubella ≥ 4 IU/mL	107			
IgG varicella antibodies ≥ 1:4 dilution	101			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroconverted for measles, mumps and rubella antibodies above the cut-off value.

End point title	Number of subjects seroconverted for measles, mumps and rubella antibodies above the cut-off value.[5]

End point description:

Seroconversion was defined as the appearance of antibodies (i.e. titer greater than or equal to the cut-off value) in the serum of subjects seronegative before vaccination. The cut-off values for seroconversion was 150 mIU/mL, 231 U/mL and 4 IU/mL for measles, mumps and rubella, respectively. This outcome measure concerns the MMR Group only.

End point type	Secondary

End point timeframe:

At 28-30 days after the first dose and 42-56 days after the second dose of MMR vaccine.

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This outcome measure concerns the MMR Group only.

End point values	MMR Group			
Subject group type	Reporting group			
Number of subjects analysed	107			
Units: Subjects				
anti-measles ≥ 150 mIU/mL; D28-30	96			
anti-measles ≥ 150 mIU/mL; D42-56	104			
anti-mumps ≥ 231 U/ML; D28-30	76			
anti-mumps ≥ 231 U/ML; D42-56	101			
anti-rubella ≥ 4 IU/mL; D28-30	98			
anti-rubella ≥ 4 IU/mL; D42-56	107			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any and grade 3 solicited local symptoms

End point title	Number of subjects reporting any and grade 3 solicited local symptoms

End point description:

Assessed solicited local symptoms were pain, redness and swelling. Any = occurrence of the symptom regardless of intensity grade. Grade 3 pain = pain that prevented normal activity. Grade 3 redness/swelling = redness/swelling spreading beyond 20 millimeters (mm) of injection site.

End point type	Secondary

End point timeframe:

Within 4 days after each vaccination (Day 0-3)

End point values	MMRV/4W Group	MMRV/12M Group	MMR Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	182	176	184	
Units: Subjects				
Any Pain; Dose 1	21	31	21	
Grade 3 Pain; Dose 1	0	1	0	
Any Redness; Dose 1	34	43	41	
Grade 3 Redness; Dose 1	1	0	1	
Any Swelling; Dose 1	10	14	16	
Grade 3 Swelling; Dose 1	0	0	0	
Any Pain; Dose 2	11	17	11	
Grade 3 Pain; Dose 2	0	2	1	
Any Redness; Dose 2	36	32	32	
Grade 3 Redness; Dose 2	1	1	1	
Any Swelling; Dose 2	13	12	14	
Grade 3 Swelling; Dose 2	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any, grade 3 and related fever

End point title	Number of subjects reporting any, grade 3 and related fever

End point description:

Any fever was defined as fever ≥ 38.0°C and grade 3 fever > 39.5°C after vaccination. Related fever was defined as fever assessed by the investigator as related to the vaccination.

End point type	Secondary

End point timeframe:

During the 15-day (Day 0-14) post-vaccination period following each dose.

End point values	MMRV/4W Group	MMRV/12M Group	MMR Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	183	179	185	
Units: Subjects				
Any temperature; Dose 1	117	88	86	
Grade 3 temperature; Dose 1	29	18	17	
Related temperature; Dose 1	69	64	51	
Any temperature; Dose 2	80	52	63	
Grade 3 temperature; Dose 2	8	7	13	
Related temperature; Dose 2	40	28	36	

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects reporting any, grade 3 and related solicited general symptoms

End point description:

Assessed solicited general symptoms were fever, meningism, parotid gland swelling and rash. Any = occurrence of the symptom regardless of intensity grade. Grade 3 parotid / salivary gland swelling = swelling with accompanying general symptoms and grade 3 rash = intensity > 150 lesions. Related = symptom assessed by the investigator as related to the vaccination.

End point type	Secondary

End point timeframe:

During the 29-day (Day 0-28) post-vaccination period following each dose.

End point values	MMRV/4W Group	MMRV/12M Group	MMR Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	183	179	185	
Units: Subjects				
Any temperature; Dose 1	124	100	99	
Grade 3 temperture; Dose 1	37	31	27	
Related temperature; Dose 1	72	67	54	
Any Meningism; Dose 1	0	0	1	
Grade 3 Meningism; Dose 1	0	0	0	
Related Meningism; Dose 1	0	0	0	
Any Parotid gland swelling; Dose 1	0	1	0	
Grade 3 Parotid gland swelling; Dose 1	0	0	0	
Related Parotid gland swelling; Dose 1	0	1	0	
Any Rash; Dose 1	29	33	35	
Grade 3 Rash; Dose 1	3	2	5	
Related Rash; Dose 1	4	6	0	
Any temperature; Dose 2	92	66	87	
Grade 3 temperature; Dose 2	12	12	30	

Related temperature; Dose 2	40	28	40	
Any Meningism; Dose 2	0	0	1	
Grade 3 Meningism; Dose 2	0	0	1	
Related Meningism; Dose 2	0	0	0	
Any Parotid gland swelling; Dose 2	0	2	0	
Grade 3 Parotid gland swelling; Dose 2	0	1	0	
Related Parotid gland swelling; Dose 2	0	1	0	
Any Rash; Dose 2	14	8	23	
Grade 3 Rash; Dose 2	1	1	6	
Related 3 Rash; Dose 2	2	0	4	

Statistical analyses

No statistical analyses for this end point

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

End point title	Number of subjects reporting any, grade 3 and related solicited general symptoms

End point description:

Assessed solicited general symptoms were fever, meningism, parotid gland swelling and rash. Any = occurrence of the symptom regardless of intensity grade. Grade 3 parotid / salivary gland swelling = swelling with accompanying general symptoms and grade 3 rash = intensity > 150 lesions. Related = symptom assessed by the investigator as related to the vaccination. This outcome measure is not applicable to subjects in MMRV/4W Group and MMR Group for Dose 1 as these subjects were administered the study vaccine during this outcome measure time frame.

End point type	Secondary

End point timeframe:

During the 43-day (Day 0-42) post-vaccination period following each dose.

End point values	MMRV/4W Group	MMRV/12M Group	MMR Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	181	179	183	
Units: Subjects				
Any temperature; Dose 1	0	106	0	
Grade 3 temperature; Dose 1	0	36	0	
Related temperature; Dose 1	0	67	0	
Any Meningism; Dose 1	0	1	0	
Grade 3 Meningism; Dose 1	0	0	0	
Related Meningism; Dose 1	0	0	0	
Any Parotid gland swelling; Dose 1	0	1	0	
Grade 3 Parotid gland swelling; Dose 1	0	0	0	
Related Parotid gland swelling; Dose 1	0	1	0	
Any Rash; Dose 1	0	37	0	
Grade 3 Rash; Dose 1	0	3	0	
Related Rash; Dose 1	0	6	0	
Any temperature; Dose 2	104	76	97	
Grade 3 temperature; Dose 2	19	18	33	

Related temperature; Dose 2	40	30	40	
Any Meningism; Dose 2	0	0	1	
Grade 3 Meningism; Dose 2	0	0	1	
Related Meningism; Dose 2	0	0	0	
Any Parotid gland swelling; Dose 2	0	2	0	
Grade 3 Parotid gland swelling; Dose 2	0	1	0	
Related Parotid gland swelling; Dose 2	0	1	0	
Any Rash; Dose 2	19	10	26	
Grade 3 Rash; Dose 2	1	1	6	
Related Rash; Dose 2	2	0	4	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicted adverse event

End point title	Number of subjects reporting any unsolicted adverse event

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. Also any 'solicited' symptom with onset outside the specified period of follow-up for solicited symptoms was reported as an unsolicited adverse event.

End point type	Secondary

End point timeframe:

Within 29 days after Dose 1.

End point values	MMRV/4W Group	MMRV/12M Group	MMR Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	184	161	185	
Units: Subjects				
any AE(s)	86	74	77	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited adverse event

End point title	Number of subjects reporting any unsolicited adverse event

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. Also any 'solicited' symptom with onset outside the specified period of follow-up for solicited symptoms was reported as an unsolicited adverse event.

End point type	Secondary

End point timeframe:

Within 43 days after Dose 1.

End point values	MMRV/4W Group	MMRV/12M Group	MMR Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	188	184	187	
Units: Subjects				
Any AE(s)	87	83	79	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited adverse event

End point title	Number of subjects reporting any unsolicited adverse event

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. Also any 'solicited' symptom with onset outside the specified period of follow-up for solicited symptoms was reported as an unsolicited adverse event.

End point type	Secondary

End point timeframe:

Within 43 days after Dose 2.

End point values	MMRV/4W Group	MMRV/12M Group	MMR Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	184	161	185	
Units: Subjects				
Any AE(s)	70	51	89	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Serious adverse events (SAEs) assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization, result in disability/incapacity or

congenital anomaly/birth defect in the offspring of a study subject.

End point type	Secondary

End point timeframe:

During the entire study period (Month 0 - Month 13.5)

End point values	MMRV/4W Group	MMRV/12M Group	MMR Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	184	161	185	
Units: Subjects				
Any SAE(s)	2	10	10	

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody titers against measles, mumps, rubella and varicella viruses

End point title	Antibody titers against measles, mumps, rubella and varicella viruses

End point description:

Antibody titers were summarized by geometric mean titers (GMTs) with their 95% CIs.

End point type	Secondary

End point timeframe:

One year post Dose 2 in Groups MMRV/4W and MMR (Month 13.5) and one year post Dose 1 in MMRV/12M Group (Month 12).

End point values	MMRV/4W Group	MMRV/12M Group	MMR Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	110	137	107	
Units: mIU/mL				
geometric mean (confidence interval 95%)				
anti-measles	4086.9 (3401.4 to 4910.7)	3759.3 (3105.9 to 4550.2)	1960.4 (1559.4 to 2464.5)	
anti-mumps	1066.9 (864.5 to 1316.6)	1116.1 (926 to 1345.3)	1045.3 (847.7 to 1289)	
anti-rubella	98.7 (83.5 to 116.8)	101.1 (86.2 to 118.6)	107.6 (91.5 to 126.6)	
IgG varicella antibodies	310.7 (237.4 to 406.7)	128 (91.3 to 179.5)	0 (0 to 0)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited local symptoms: within 4 days after each vaccination, solicited general symptoms: during the 29-day and during the 43-day post-vaccination after each dose. Unsolicited AEs: 43 days after Dose 1&2. SAEs: Month 0 - Month 13.5

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	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	11

Reporting groups

Reporting group title	MMRV/4W Group

Reporting group description:

Subjects received two doses of MMRV vaccine 4 weeks apart (Day 0 and Week 4).

Reporting group title	MMRV/12M Group

Reporting group description:

Subjects received two doses of Priorix™-Tetra vaccine (MMRV) 12 months apart (Day 0 and Month 12).

Reporting group title	MMR Group

Reporting group description:

Subjects received two doses of Priorix™ vaccine (MMR) 4 weeks apart (Day 0 and Week 4)

Serious adverse events	MMRV/4W Group	MMRV/12M Group	MMR Group
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 188 (1.06%)	10 / 184 (5.43%)	10 / 187 (5.35%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Brain contusion			
alternative assessment type: Non-systematic			
subjects affected / exposed[1]	0 / 184 (0.00%)	1 / 161 (0.62%)	0 / 185 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug toxicity			
alternative assessment type: Non-systematic			

subjects affected / exposed[2]	0 / 184 (0.00%)	0 / 161 (0.00%)	1 / 185 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Febrile convulsion			
alternative assessment type: Non-systematic			
subjects affected / exposed[3]	0 / 184 (0.00%)	2 / 161 (1.24%)	1 / 185 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Convulsion			
alternative assessment type: Non-systematic			
subjects affected / exposed[4]	0 / 184 (0.00%)	0 / 161 (0.00%)	1 / 185 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Gait disturbance			
alternative assessment type: Non-systematic			
subjects affected / exposed[5]	0 / 184 (0.00%)	1 / 161 (0.62%)	0 / 185 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Lymphadenitis			
alternative assessment type: Non-systematic			
subjects affected / exposed[6]	0 / 184 (0.00%)	0 / 161 (0.00%)	1 / 185 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Concussion			
subjects affected / exposed[7]	0 / 184 (0.00%)	1 / 161 (0.62%)	0 / 185 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Bronchitis chronic			
alternative assessment type: Non-systematic			

subjects affected / exposed[8]	0 / 184 (0.00%)	1 / 161 (0.62%)	1 / 185 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pneumonia			
alternative assessment type: Non-systematic			
subjects affected / exposed[9]	1 / 184 (0.54%)	1 / 161 (0.62%)	2 / 185 (1.08%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis rotavirus			
alternative assessment type: Non-systematic			
subjects affected / exposed[10]	0 / 184 (0.00%)	1 / 161 (0.62%)	2 / 185 (1.08%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
alternative assessment type: Non-systematic			
subjects affected / exposed[11]	0 / 184 (0.00%)	1 / 161 (0.62%)	0 / 185 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
alternative assessment type: Non-systematic			
subjects affected / exposed[12]	0 / 184 (0.00%)	1 / 161 (0.62%)	0 / 185 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infectious mononucleosis			
alternative assessment type: Non-systematic			
subjects affected / exposed[13]	0 / 184 (0.00%)	1 / 161 (0.62%)	0 / 185 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			
alternative assessment type: Non-systematic			

subjects affected / exposed[14]	1 / 184 (0.54%)	0 / 161 (0.00%)	0 / 185 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudocroup			
alternative assessment type: Non-systematic			
subjects affected / exposed[15]	0 / 184 (0.00%)	1 / 161 (0.62%)	0 / 185 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
alternative assessment type: Non-systematic			
subjects affected / exposed[16]	0 / 184 (0.00%)	1 / 161 (0.62%)	0 / 185 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 1 diabetes mellitus			
alternative assessment type: Non-systematic			
subjects affected / exposed[17]	0 / 184 (0.00%)	0 / 161 (0.00%)	1 / 185 (0.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[10] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[11] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[12] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[13] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[14] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[15] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[16] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[17] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

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

Non-serious adverse events	MMRV/4W Group	MMRV/12M Group	MMR Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	124 / 188 (65.96%)	106 / 184 (57.61%)	99 / 187 (52.94%)
Injury, poisoning and procedural complications			
Upper respiratory tract infection; Dose 1	Additional description: Within 43 days after Dose 1		
subjects affected / exposed	12 / 188 (6.38%)	19 / 184 (10.33%)	7 / 187 (3.74%)
occurrences (all)	12	19	7
General disorders and administration site conditions			
Pain; Dose 1			
subjects affected / exposed[18]	21 / 182 (11.54%)	31 / 176 (17.61%)	21 / 184 (11.41%)
occurrences (all)	21	31	21
Redness; Dose 1			
subjects affected / exposed[19]	34 / 182 (18.68%)	43 / 176 (24.43%)	41 / 184 (22.28%)
occurrences (all)	34	43	41
Swelling; Dose 1			
subjects affected / exposed[20]	10 / 182 (5.49%)	14 / 176 (7.95%)	16 / 184 (8.70%)
occurrences (all)	10	14	16
Pain; Dose 2			
subjects affected / exposed[21]	11 / 179 (6.15%)	17 / 156 (10.90%)	11 / 180 (6.11%)
occurrences (all)	11	17	11
Redness; Dose 2			
subjects affected / exposed[22]	36 / 179 (20.11%)	32 / 156 (20.51%)	32 / 180 (17.78%)
occurrences (all)	36	32	32
Swelling; Dose 2			
subjects affected / exposed[23]	13 / 179 (7.26%)	12 / 156 (7.69%)	14 / 180 (7.78%)
occurrences (all)	13	12	14
Fever; Dose 1 (D0-28)	Additional description: Reported during the 29-day (Day 0-28) post-vaccination period following dose 1.		
subjects affected / exposed[24]	124 / 183 (67.76%)	100 / 179 (55.87%)	99 / 185 (53.51%)
occurrences (all)	124	100	99
Rash; Dose 1 (D0-28)	Additional description: Reported during the 29-day (Day 0-28) post-vaccination period following dose 1.		
subjects affected / exposed[25]	29 / 183 (15.85%)	33 / 179 (18.44%)	35 / 185 (18.92%)
occurrences (all)	29	33	35
Fever; Dose 2 (D0-42)	Additional description: Reported during the 43-day (Day 0-42) post-vaccination period following dose 2.		

subjects affected / exposed[26]	104 / 181 (57.46%)	76 / 155 (49.03%)	97 / 183 (53.01%)
occurrences (all)	104	76	97
Rash; Dose 2 (D0-42)	Additional description: Reported during the 43-day (Day 0-42) post-vaccination period following dose 2.		
subjects affected / exposed[27]	19 / 181 (10.50%)	10 / 155 (6.45%)	26 / 183 (14.21%)
occurrences (all)	19	10	26
Fever; Dose 2 (D0-28)	Additional description: Reported during the 29-day (Day 0-28) post-vaccination period following dose 2.		
subjects affected / exposed[28]	92 / 181 (50.83%)	66 / 155 (42.58%)	87 / 183 (47.54%)
occurrences (all)	92	66	87
Rash; Dose 2 (D0-28)	Additional description: Reported during the 29-day (Day 0-28) post-vaccination period following dose 2.		
subjects affected / exposed[29]	14 / 181 (7.73%)	8 / 155 (5.16%)	23 / 183 (12.57%)
occurrences (all)	14	8	23
Fever; Dose 1 (D0-42)	Additional description: Reported during the 43-day post-vaccination period following dose 1.This symptom was reported by subjects in the MMRV/12M Group only & is not applicable to subjects in MMRV/4W & MMR Groups due to another vaccination planned for these subjects.		
subjects affected / exposed[30]	0 / 188 (0.00%)	106 / 179 (59.22%)	0 / 187 (0.00%)
occurrences (all)	0	106	0
Rash; Dose 1 (D0-42)	Additional description: Reported during the 43-day post-vaccination period following dose 1.This symptom was reported by subjects in the MMRV/12M Group only & is not applicable to subjects in MMRV/4W & MMR Groups due to another vaccination planned for these subjects.		
subjects affected / exposed[31]	0 / 188 (0.00%)	37 / 179 (20.67%)	0 / 187 (0.00%)
occurrences (all)	0	37	0
Gastrointestinal disorders			
Teething; Dose 2	Additional description: Within 43 days after Dose 2		
alternative assessment type: Non-systematic			
subjects affected / exposed[32]	10 / 184 (5.43%)	0 / 161 (0.00%)	7 / 185 (3.78%)
occurrences (all)	10	0	7
Respiratory, thoracic and mediastinal disorders			
Cough; Dose 1	Additional description: Within 43 days after Dose 1		
subjects affected / exposed	16 / 188 (8.51%)	5 / 184 (2.72%)	5 / 187 (2.67%)
occurrences (all)	16	5	5
Infections and infestations			
Gastroenteritis; Dose 1	Additional description: Within 43 days after Dose 1		
subjects affected / exposed	8 / 188 (4.26%)	14 / 184 (7.61%)	10 / 187 (5.35%)
occurrences (all)	8	14	10
Rhinitis; Dose 1	Additional description: Within 43 days after Dose 1		
subjects affected / exposed	10 / 188 (5.32%)	8 / 184 (4.35%)	10 / 187 (5.35%)
occurrences (all)	10	8	10

Bronchitis; Dose 1	Additional description: Within 43 days after Dose 1		
subjects affected / exposed	5 / 188 (2.66%)	16 / 184 (8.70%)	9 / 187 (4.81%)
occurrences (all)	5	16	9
Nasopharyngitis; Dose 1	Additional description: Within 43 days after Dose 1		
subjects affected / exposed	8 / 188 (4.26%)	0 / 184 (0.00%)	12 / 187 (6.42%)
occurrences (all)	8	0	12
Gastroenteritis; Dose 2	Additional description: Within 43 days after Dose 2		
alternative assessment type: Non-systematic			
subjects affected / exposed[33]	14 / 184 (7.61%)	6 / 161 (3.73%)	11 / 185 (5.95%)
occurrences (all)	14	6	11
Upper respiratory tract infection; Dose 2	Additional description: Within 43 days after Dose 2		
alternative assessment type: Non-systematic			
subjects affected / exposed[34]	8 / 184 (4.35%)	9 / 161 (5.59%)	9 / 185 (4.86%)
occurrences (all)	8	9	9
Bronchitis; Dose 2	Additional description: Within 43 days after Dose 2		
alternative assessment type: Non-systematic			
subjects affected / exposed[35]	6 / 184 (3.26%)	7 / 161 (4.35%)	11 / 185 (5.95%)
occurrences (all)	6	7	11
Nasopharyngitis; Dose 2	Additional description: Within 43 days after Dose 2		
alternative assessment type: Non-systematic			
subjects affected / exposed[36]	7 / 184 (3.80%)	5 / 161 (3.11%)	10 / 185 (5.41%)
occurrences (all)	7	5	10
Otitis media; Dose 1	Additional description: Within 43 days after Dose 1		
alternative assessment type: Non-systematic			
subjects affected / exposed	9 / 188 (4.79%)	10 / 184 (5.43%)	9 / 187 (4.81%)
occurrences (all)	9	10	9
Otitis media; Dose 2	Additional description: Within 43 days after Dose 2		
alternative assessment type: Non-systematic			
subjects affected / exposed[37]	5 / 184 (2.72%)	6 / 161 (3.73%)	11 / 185 (5.95%)
occurrences (all)	5	6	11

Notes:

[18] - 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: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

[19] - 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: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[20] - 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: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[21] - 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: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[22] - 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: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[23] - 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: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[24] - 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: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[25] - 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: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[26] - 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: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[27] - 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: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[28] - 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: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[29] - 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: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[30] - 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: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[31] - 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: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[32] - 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: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant

medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[33] - 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: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[34] - 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: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[35] - 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: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[36] - 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: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).
[37] - 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: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively).

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