Clinical trial results:
Immunogenicity and safety study of GSK Biologicals' combined measles-mumps-rubella vaccine in subjects seven years and older (209762).

Summary

EudraCT number	2011-003672-36
Trial protocol	SK EE
Global end of trial date	17 September 2015

Results information

Result version number	v2 (current)
This version publication date	12 March 2017
First version publication date	15 January 2017
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	115231

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02058563
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, 44 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, 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?	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	08 July 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	24 May 2015
Global end of trial reached?	Yes
Global end of trial date	17 September 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the non-inferiority of INV_MMR vaccine to COM_MMR vaccine in terms of Geometric Mean Concentration (GMCs) for anti measles, anti mumps and anti rubella antibodies at Day 42. Criteria for the determination of non-inferiority for measles, mumps, and rubella viruses: Lower limit (LL) of the 2-sided 95% Confidence Interval (CI) on GMC ratio (INV_MMR over COM_MMR) is equal to or above 0.67 for anti-measles, anti-mumps, and anti rubella antibodies.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 July 2014
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	Slovakia: 216
Country: Number of subjects enrolled	United States: 671
Country: Number of subjects enrolled	Estonia: 109
Worldwide total number of subjects	996
EEA total number of subjects	325

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)	0
Children (2-11 years)	250
Adolescents (12-17 years)	84
Adults (18-64 years)	661

From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 996 subjects were enrolled and 994 were vaccinated. Of the 994 vaccinated subjects, 83 subjects from 2 US site s were excluded due to significant GCP concerns, resulting in 911 subjects in the Total vaccinated cohort considered for the analysis.

Pre-assignment

Screening details:

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.

Pre-assignment period milestones

Number of subjects started	996
Number of subjects completed	911

Pre-assignment subject non-completion reasons

Reason: Number of subjects	excluded due to GCP concerns: 83
Reason: Number of subjects	subjects non vaccinated: 2

Period 1

Period 1 title	Overall study period (Day 0 to Day 180) (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Blinding implementation details:

Data will be collected in an observer-blind manner. By observer-blind, it is meant that during the course of the study, the vaccine recipient and those responsible for the evaluation of any study endpoint (e.g. safety, reactogenicity, and efficacy) will all be unaware of which vaccine was administered. To do so, vaccine preparation and administration will be done by authorized medical personnel who will not participate in any of the study clinical evaluations.

Arms

Are arms mutually exclusive?	Yes
Arm title	INV_MMR Group

Arm description:

Subjects received one dose of INV_MMR (Priorix®) vaccine at Visit 1 (Day 0).

Arm type	Experimental
Investigational medicinal product name	Priorix
Investigational medicinal product code	209762
Other name	MEASLES VIRUS SCHWARZ STRAIN (LIVE, ATTENUATED); INV_MMR
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

A single vaccination was given on study Day 0 in the “triceps” region of the upper arm.

Arm title	COM_MMR Group

Arm description:

Subjects received one dose of COM_MMR (M-M-R®II) vaccine from Lot 1 or Lot 2 at Visit 1 (Day 0).

Arm type	Active comparator

Investigational medicinal product name	M-M-R VAXPRO
Investigational medicinal product code	
Other name	COM_MMR
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

A single vaccination was given on study Day 0 in the “triceps” region of the upper arm.

Number of subjects in period 1[1]	INV_MMR Group	COM_MMR Group
Started	454	457
Completed	426	433
Not completed	28	24
Consent withdrawn by subject	1	1
Patient incarcerated	-	1
Lost to follow-up	26	22
Vaccinated later as new subject	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: A total of 996 subjects were enrolled and 994 were vaccinated. Of the 994 vaccinated subjects, 83 subjects from 2 US sites were excluded due to significant GCP concerns, resulting in 911 subjects in the Total vaccinated cohort considered for the analysis.

Baseline characteristics

Reporting groups	
Reporting group title	INV_MMR Group
Reporting group description:	
Subjects received one dose of INV_MMR (Priorix®) vaccine at Visit 1 (Day 0).	
Reporting group title	COM_MMR Group
Reporting group description:	
Subjects received one dose of COM_MMR (M-M-R®II) vaccine from Lot 1 or Lot 2 at Visit 1 (Day 0).	

Reporting group values	INV_MMR Group	COM_MMR Group	Total
Number of subjects	454	457	911
Age categorical Units: Subjects			
Age continuous			
Age continuous description			
Units: years			
arithmetic mean	25.9	25.6	
standard deviation	± 13.9	± 13.8	-
Gender categorical			
Gender categorical description			
Units: Subjects			
Female	250	252	502
Male	204	205	409
Race/Ethnicity, Customized Units: Subjects			
African Heritage/African American	108	103	211
American Indian or Alaskan native	2	4	6
Asian - Central/South Asian heritage	1	0	1
Asian - East Asian heritage	1	0	1
Asian - Japanese heritage	0	1	1
Asian - South East Asian heritage	0	0	0
Native Hawaiian or other Pacific Islander	1	0	1
White - Arabic/North African heritage	0	1	1
White - Caucasian/European heritage	334	344	678
Other	7	4	11

End points

End points reporting groups

Reporting group title	INV_MMR Group
Reporting group description:	
Subjects received one dose of INV_MMR (Priorix®) vaccine at Visit 1 (Day 0).	
Reporting group title	COM_MMR Group
Reporting group description:	
Subjects received one dose of COM_MMR (M-M-R®II) vaccine from Lot 1 or Lot 2 at Visit 1 (Day 0).	

Primary: Anti-measles virus antibody Concentrations

End point title	Anti-measles virus antibody Concentrations
End point description:	
Antibody concentrations are expressed as Geometric Mean Concentrations (GMCs) in milli International Units per milliliter (mIU/mL). Seropositivity was defined as subjects with anti-measles virus antibody concentration equal or greater than 150 mIU/mL.	
End point type	Primary
End point timeframe:	
At Day 42	

End point values	INV_MMR Group	COM_MMR Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	433	436		
Units: mIU/mL				
geometric mean (confidence interval 95%)	1795.6 (1641.1 to 1964.7)	1783.3 (1624.6 to 1957.4)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description:	
Non-inferiority of INV_MMR vaccine to COM_MMR vaccine in terms of Geometric Mean Concentration (GMCs) for anti measles, anti mumps and anti rubella antibodies at Day 42.The 95% CI for adjusted geometric mean concentrations (GMCs) and the adjusted GMC ratio were obtained using an ANCOVA model on the logarithm-transformed concentrations including the vaccine group (for adjusted GMC ratio) as fixed effect, gender, age and country groups as continuous effects and the pre-vaccination log-transformed	
Comparison groups	INV_MMR Group v COM_MMR Group

Number of subjects included in analysis	869
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Adjusted GMC ratio
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.91
upper limit	1.11

Notes:

[1] - Criteria for the determination of non-inferiority for measles, mumps, and rubella viruses: Lower limit (LL) of the 2-sided 95% Confidence Interval (CI) on GMC ratio ((INV_MMR over COM_MMR) was to be equal to or above 0.67 for anti-measles, anti-mumps, and anti rubella antibodies. Number of subjects in INV-MMR Group and in COM-MMR Group considered for calculating the adjusted GMC ratio, are 432 and 435 and adjusted GMCs = 1790.2 (LL=1669.6;UL=1919.5) and 1781.5 (LL=1661.8;UL=1909.7) respectively

Primary: Anti-mumps virus antibody Concentrations

End point title	Anti-mumps virus antibody Concentrations

End point description:

Antibody concentrations are expressed as Geometric Mean Concentrations (GMCs) in EU/mL. Seropositivity was defined as subjects with anti-mumps virus antibody concentration equal or greater than 5 EU/mL.

End point type	Primary

End point timeframe:

At Day 42

End point values	INV_MMR Group	COM_MMR Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	433	436		
Units: EU/mL				
geometric mean (confidence interval 95%)	110.6 (102.1 to 119.8)	110.2 (101.9 to 119.2)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Non-inferiority of INV_MMR vaccine to COM_MMR vaccine in terms of Geometric Mean Concentration (GMCs) for anti measles, anti mumps and anti rubella antibodies at Day 42.The 95% CI for adjusted geometric mean concentrations (GMCs) and the adjusted GMC ratio were obtained using an ANCOVA model on the logarithm-transformed concentrations including the vaccine group (for adjusted GMC ratio) as fixed effect, gender, age and country groups as continuous effects and the pre-vaccination log-transformed.

Comparison groups	COM_MMR Group v INV_MMR Group

Number of subjects included in analysis	869
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Adjusted GMC ratio
Point estimate	1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.96
upper limit	1.16

Notes:

[2] - Criteria for the determination of non-inferiority for measles, mumps, and rubella viruses: Lower limit (LL) of the 2-sided 95% Confidence Interval (CI) on GMC ratio (INV_MMR over COM_MMR) was to be equal to or above 0.67 for anti-measles, anti-mumps, and anti rubella antibodies. Number of subjects in INV-MMR Group and in COM-MMR Group considered for calculating the adjusted GMC ratio, are 432 and 435 and adjusted GMCs = 113.5 (LL=106.0;UL=121.6) and 107.8 (LL=100.7;UL=115.4) respectively.

Primary: Anti-rubella virus antibody Concentrations

End point title	Anti-rubella virus antibody Concentrations

End point description:

Antibody concentrations are expressed as Geometric Mean Concentrations (GMCs) in IU/mL. Seropositivity was defined as subjects with anti-rubella virus antibody concentration equal or greater than 4 IU/mL.

End point type	Primary

End point timeframe:

At Day 42

End point values	INV_MMR Group	COM_MMR Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	433	436		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Reporting groups	75.3 (70.3 to 80.6)	75.6 (70.8 to 80.7)		

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

Non-inferiority of INV_MMR vaccine to COM_MMR vaccine in terms of Geometric Mean Concentration (GMCs) for anti measles, anti mumps and anti rubella antibodies at Day 42.The 95% CI for adjusted geometric mean concentrations (GMCs) and the adjusted GMC ratio were obtained using an ANCOVA model on the logarithm-transformed concentrations including the vaccine group (for adjusted GMC ratio) as fixed effect, gender, age and country groups as continuous effects and the pre-vaccination log-transformed

Comparison groups	COM_MMR Group v INV_MMR Group

Number of subjects included in analysis	869
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Adjusted GMC ratio
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	1.11

Notes:

[3] - Criteria for the determination of non-inferiority for measles, mumps, and rubella viruses: Lower limit (LL) of the 2-sided 95% Confidence Interval (CI) on GMC ratio (INV_MMR over COM_MMR) was to be equal to or above 0.67 for anti-measles, anti-mumps, and anti rubella antibodies. Number of subjects in the INV-MMR Group and in the COM-MMR Group considered for calculating the adjusted GMC ratio, are 432 and 435 and adjusted GMCs = 76.1 (LL=71.5;UL=81.0) and 74.6 (LL=70.2;UL=79.4) respectively.

Secondary: Number of subjects with anti-measles virus antibody concentration equal to or above the threshold of 200 mIU/mL (seroresponse rate)

End point title	Number of subjects with anti-measles virus antibody concentration equal to or above the threshold of 200 mIU/mL (seroresponse rate)

End point description:

Seroresponse was defined as: Anti-measles virus antibody concentration equal to or above the threshold of 200 mIU/mL after administration of INV_MMR vaccine vs. COM_MMR at Day 42

End point type	Secondary

End point timeframe:

At Day 42

End point values	INV_MMR Group	COM_MMR Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	433	436		
Units: Subjects	428	432		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-mumps virus antibody concentration equal to or above the threshold of 10 EU/mL (seroresponse rate).

End point title	Number of subjects with anti-mumps virus antibody concentration equal to or above the threshold of 10 EU/mL (seroresponse rate).

End point description:

Seroresponse was defined as: Anti-mumps virus antibody concentration equal to or above the threshold of 10 EU/mL after administration of INV_MMR vaccine vs. COM_MMR at Day 42.

End point type	Secondary

End point timeframe:

At Day 42

End point values	INV_MMR Group	COM_MMR Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	433	436		
Units: Subjects	426	434		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-rubella virus antibody concentration equal to or above the threshold of 10 IU/mL (seroresponse rate).

End point title	Number of subjects with anti-rubella virus antibody concentration equal to or above the threshold of 10 IU/mL (seroresponse rate).

End point description:

Seroresponse was defined as: Anti-rubella virus antibody concentration equal to or above the threshold of 10 IU/mL after administration of INV_MMR vaccine vs. COM_MMR at Day 42.

End point type	Secondary

End point timeframe:

At Day 42

End point values	INV_MMR Group	COM_MMR Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	433	436		
Units: Subjects	431	435		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects who achieved a 4-fold or greater rise in anti-measles, anti-mumps and anti-rubella virus antibody concentrations.

End point title	Number of subjects who achieved a 4-fold or greater rise in anti-measles, anti-mumps and anti-rubella virus antibody concentrations.

End point description:

For subjects with seronegative status at pre-vaccination, a 4-fold rise in antibody concentration is defined as 4 times the cut-off level of the assay. Cut-off levels for anti-measles, anti-mumps and anti-rubella virus antibody concentrations are 150 m IU/mL, 5 EU/mL and 4 IU/mL.

End point type	Secondary

End point timeframe:

At Day 42

End point values	INV_MMR Group	COM_MMR Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	432	435		
Units: Subjects				
Anti-measles	42	48		
Anti-mumps	152	128		
Anti-rubella	179	161		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited local symptoms

End point title	Number of subjects with solicited local symptoms

End point description:

Assessed solicited local symptoms were pain, redness and swelling. Any = Occurrence of any local symptom regardless of its intensity grade. Grade 3 Pain = Significant pain at rest. Prevented normal every day activities. Grade 3 redness = redness with surface diameter >50mm. Grade 3 swelling = swelling with surface diameter >50mm.

End point type	Secondary

End point timeframe:

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

End point values	INV_MMR Group	COM_MMR Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	433	445		
Units: Subjects				
Any injection site redness	53	52		
Grade 3 injection site redness	0	0		
Any injection site swelling	23	29		
Grade 3 injection site swelling	0	0		
Any injection site pain	51	51		
Grade 3 injection site pain	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting fever

End point title	Number of subjects reporting fever

End point description:

Fever was assessed:Any fever (≥38°C) = occurrence of any fever regardless of its intensity grade or relationship to vaccination. Grade3 fever = fever >39.5°C. . Related = symptom assessed by the investigator as causally related to study vaccination.The preferred route for recording temperature in this study was oral.

End point type	Secondary

End point timeframe:

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

End point values	INV_MMR Group	COM_MMR Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	431	445		
Units: Subjects				
Any	13	23		
Grade 3	1	6		
Related	2	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited general symptoms as parotid/salivary gland swelling and any sign of meningism /seizure.

End point title	Number of subjects reporting solicited general symptoms as parotid/salivary gland swelling and any sign of meningism /seizure.

End point description:

Assessed MMR specific symptoms were parotid/salivary gland swelling and any sign of meningism /seizure.
Parotid/salivary gland swelling: Any = occurrence of any general symptom regardless of its intensity grade or relationship to vaccination; Grade 3 Parotid/salivary gland swelling = Swelling accompanied with general symptoms. Meningism /seizure: Any= occurrence of any general symptom regardless of its intensity grade or relationship to vaccination; Grade-3 meningism /seizure= Prevented normal, everyday activities (In adults/adolescents, such an AE could, for example, prevented attendance at work/school and could necessitated the administration of corrective therapy). Related symptom = symptom assessed by the investigator as causally related to study vaccination.

End point type	Secondary

End point timeframe:

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

End point values	INV_MMR Group	COM_MMR Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	431	445		
Units: Subjects				
Any parotid/salivary gland swelling	1	1		
Grade 3 parotid/salivary gland swelling	1	0		
Related parotid/salivary gland swelling	0	0		
Any meningism/seizure	1	1		
Grade 3 meningism/seizure	1	0		
Related meningism/seizure	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting unsolicited AEs

End point title	Number of subjects reporting unsolicited AEs

End point description:

Any untoward medical occurrence in a patient or clinical investigation child, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product

End point type	Secondary

End point timeframe:

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

End point values	INV_MMR Group	COM_MMR Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	454	457		
Units: Subjects	95	82		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited rash symptom.

End point title	Number of subjects reporting solicited rash symptom.

End point description:

Assessed any rash, Grade 3, Related, Localized rash, Generalized rash,measles/rubella-rash. Any= occurrence of any general symptom regardless of its intensity grade or relationship to vaccination. Grade3 rash/exanthema= Rash which prevented normal, everyday activities (In adults/adolescents, such an AE could, for example, prevented attendance at work/school and could necessitated the administration of corrective therapy). Grade 3 measles/rubella/varicella-like rash = Rash with more than150 lesions. Related = symptom assessed by the investigator as causally related to study vaccination.

End point type	Secondary

End point timeframe:

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

End point values	INV_MMR Group	COM_MMR Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	431	445		
Units: Subjects				
Any	9	5		
Grade 3	0	0		
Related	6	2		
Localized rash	8	3		
Generalized rash	1	2		
Rash type - measles/rubella-rash	0	2		
Rash type - others	9	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited joint pain (arthralgia/arthritis)

End point title	Number of subjects reporting solicited joint pain (arthralgia/arthritis)

End point description:

Assessed any, Grade-3, Related. Any= occurrence of any general symptom regardless of its intensity grade or relationship to vaccination Grade3 joint pain (arthralgia/arthritis)= Pain which prevented normal, everyday activities (In adults/adolescents, such an AE could, for example, prevented attendance at work/school and could necessitated the administration of corrective therapy). Related = symptom assessed by the investigator as causally related to study vaccination.

End point type	Secondary

End point timeframe:

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

End point values	INV_MMR Group	COM_MMR Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	431	445		
Units: subjects				
Any	8	4		
Grade 3	0	0		
Related	3	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting NOCDs

End point title	Number of subjects reporting NOCDs

End point description:

Occurrence of new onset chronic diseases (NOCDs)

End point type	Secondary

End point timeframe:

Day 0 through the end of the study (Day 180)

End point values	INV_MMR Group	COM_MMR Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	454	457		
Units: Subjects	2	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting adverse events prompting ER visits

End point title	Number of subjects reporting adverse events prompting ER visits

End point description:

Occurrence of AEs prompting emergency room (ER) visits.

End point type	Secondary

End point timeframe:

Day 0 through the end of the study (Day 180)

End point values	INV_MMR Group	COM_MMR Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	454	457		
Units: Subjects	14	9		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

A serious adverse event (SAE) is any untoward medical occurrence that results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization or results in disability/incapacity.

End point type	Secondary

End point timeframe:

Day 0 through the end of the study (Day 180)

End point values	INV_MMR Group	COM_MMR Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	454	457		
Units: Subjects	3	7		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious Adverse Events: From Day 0 to Day 180,
Solicited Local Adverse Events: From Day 0 to Day 3,
Solicited General and Unsolicited Adverse Events: From Day 0 to Day 42

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	INV_MMR Group

Reporting group description:

Subjects received one dose of INV_MMR (Priorix®) vaccine at Visit 1 (Day 0).

Reporting group title	COM_MMR Group

Reporting group description:

Subjects received one dose of COM_MMR (M-M-R®II) vaccine from Lot 1 or Lot 2 at Visit 1 (Day 0).

Serious adverse events	INV_MMR Group	COM_MMR Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 454 (0.66%)	7 / 457 (1.53%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 454 (0.00%)	1 / 457 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Jaw fracture			
subjects affected / exposed	0 / 454 (0.00%)	1 / 457 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon injury			
subjects affected / exposed	1 / 454 (0.22%)	0 / 457 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal			

conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 454 (0.00%)	2 / 457 (0.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 454 (0.00%)	1 / 457 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain lower			
subjects affected / exposed	1 / 454 (0.22%)	0 / 457 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis relapsing			
subjects affected / exposed	0 / 454 (0.00%)	1 / 457 (0.22%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	1 / 454 (0.22%)	0 / 457 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Psychogenic seizure			
subjects affected / exposed	1 / 454 (0.22%)	0 / 457 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pyelonephritis			
subjects affected / exposed	0 / 454 (0.00%)	1 / 457 (0.22%)	
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	INV_MMR Group	COM_MMR Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	93 / 454 (20.48%)	102 / 457 (22.32%)	
General disorders and administration site conditions			
Injection site erythema			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	53 / 454 (11.67%)	52 / 457 (11.38%)	
occurrences (all)	53	52	
Injection site swelling			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	23 / 454 (5.07%)	29 / 457 (6.35%)	
occurrences (all)	23	29	
Pyrexia			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	13 / 454 (2.86%)	23 / 457 (5.03%)	
occurrences (all)	13	23	
Vaccination site pain			
alternative dictionary used: MedDRA 18.0			
subjects affected / exposed	51 / 454 (11.23%)	51 / 457 (11.16%)	
occurrences (all)	51	51	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
12 November 2013	The study has been changed in design based on the United States (US) Food and Drug Administration (FDA) Center for Biologics Evaluation and Research (CBER) feedback, highlighting the heterogeneous nature of the study population in terms of prior vaccination with a measles-containing vaccine and the possibility of providing 1 or 2 doses of measles, mumps and rubella vaccine (MMR) as part of this study. The study has therefore been simplified to evaluate the administration of 1 dose of MMR vaccine only. Prior receipt of at least 1 dose of MMR has been added as a study inclusion criterion. Whereas children 7 17 years of age will be excluded if they have received more than 1 dose of MMR vaccine, adults 18 years of age and older will be able to enroll with a verbal or written history of 1 or more doses of MMR vaccine. Prior MMR vaccination status will be recorded at baseline. Due to CBER's request to add a confirmatory objective for geometric mean concentration (GMC) ratio, the sample size has been increased in order to maintain statistical power. Since the change in study design includes only a one-dose cohort, all assessments and schedules in the study now refer to a single vaccination at Day 0, a safety follow up visit (Visit 2) at Day 42, and a phone contact at Day 180. In the interest of safety, definitions and categories of solicited local and general adverse events have been refined. The protocol has also been revised to include the offer of a rescue plan for subjects that fail to meet the seroresponse threshold for antibodies to measles, mumps or rubella virus components. Descriptive secondary statistical analyses have been added.
29 September 2014	The Dominican Republic will not be participating in the study as originally planned; therefore, all references to that country are deleted. Based on PAREXEL's site assessment and feasibility, the ex-United States (US) sites are willing and able to adjust their enrollment goals to include the pediatric subjects originally allocated to the Dominican Republic. Consequently, changes are made to pediatric enrollment figures for ex-US sites. Exclusion criterion 7 was amended to include more specific instructions regarding the administration of live influenza vaccine during the study. Minor administrative changes have been made to align this protocol with other protocols in the MMR program. These include changes to clarify the recording of adverse events and concomitant medication/vaccination, amending Table 14 for the recording of AEs, SAEs, and pregnancy; and clarification of the recording of rash events.
08 March 2015	Due to a delay in the availability of serologic data, the study team has decided to conduct one final analysis at study end, therefore eliminating the two-step analysis.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported