

**Clinical trial results:**

A phase IIIA, randomized, observer-blind, controlled, multinational study to evaluate the safety and immunogenicity of GSK Biologicals' MMR vaccine (209762) (Priorix®) compared to Merck & Co., Inc.'s MMR vaccine (MMR®II or VaxPro), as a first dose, both co-administered with Varivax, Havrix (all subjects) and Prevnar 13 (US subset) in healthy children 12 to 15 months of age

Summary

EudraCT number	2011-006161-18
Trial protocol	EE FI
Global end of trial date	22 December 2015

Results information

Result version number	v1
This version publication date	12 January 2017
First version publication date	12 January 2017

Trial information**Trial identification**

Sponsor protocol code	115650
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02184572
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium,
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	22 December 2015
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	22 December 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To demonstrate the safety profile (fever $>39.0^{\circ}\text{C}$ ($>102.2^{\circ}\text{F}$)) of Inv_MMR compared to Com_MMR (pooled lots) when co-administered with VV and HAV (to all children) and PCV-13 (only to children enrolled in the US).
- To demonstrate the safety profile (fever $\geq 38.0^{\circ}\text{C}$ ($\geq 100.4^{\circ}\text{F}$)) of Inv_MMR compared to Com_MMR (pooled lots) when co-administered with VV and HAV (to all children) and PCV-13 (children enrolled in the US).

Protection of trial subjects:

All subjects were supervised for at least 30 min after vaccination/product administration with appropriate medical treatment readily available. Vaccines/products were administered by qualified and trained personnel. Vaccines/products were administered only to eligible subjects that had no contraindications to any components of the vaccines/products.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	25 August 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	Estonia: 240
Country: Number of subjects enrolled	Finland: 220
Country: Number of subjects enrolled	Puerto Rico: 23
Country: Number of subjects enrolled	Taiwan: 185
Country: Number of subjects enrolled	United States: 1075
Worldwide total number of subjects	1743
EEA total number of subjects	460

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	1743

months)	
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:

US sub-cohort: Subjects recruited in US received INV_MMR (Priorix®) or COM_MMR (M-M-R®II/M-M-R Vax Pro™) co-administered with Varivax®, Havrix® & Prevnar 13 vaccines (Day 0). Non-US sub-cohort: Subjects recruited outside the US received INV_MMR (Priorix®) or COM_MMR (M-M-R®II/M-M-R Vax Pro™) co-administered with Varivax® & Havrix® vaccines (Day 0).

Pre-assignment period milestones

Number of subjects started	1742 ^[1]
Number of subjects completed	1736

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Subject no. allocated vaccine not administered: 6
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Notes:

[1] - The number of subjects reported to have started the pre-assignment period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: Out of 1743 subjects enrolled, 1 subject was removed from the study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Blinding implementation details:

Observer blinded study

Arms

Are arms mutually exclusive?	Yes
Arm title	INV_MMR

Arm description:

Subjects received 1 dose of the study vaccine Priorix® co administered with Varivax® and Havrix® vaccines at Day 0. Subjects recruited in the US also received Prevnar 13® at Day 0.

Arm type	Experimental
Investigational medicinal product name	Priorix®
Investigational medicinal product code	
Other name	GSK Biologicals' measles, mumps, and rubella vaccine live
Pharmaceutical forms	Powder and solvent for solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

1 dose administered subcutaneously (SC) in the tricep region of left arm.

Investigational medicinal product name	Havrix®
Investigational medicinal product code	SUB38555
Other name	Havrix junior 720 (GSK Biological Hepatitis A virus antigen (HAV))
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose administered intramuscularly (IM) in the anterolateral region of the right thigh at Visit 1 (Day 0),

with either Inv_MMR vaccine or one of the two Com_MMR vaccine lots.

Investigational medicinal product name	Varivax®
Investigational medicinal product code	SUB25312
Other name	Merck & Co. Inc.'s Live attenuated Varicella
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose administered SC in the tricep region of right arm at Visit 1 (Day 0), with either Priorix® vaccine or one of the two M-M-R®II vaccine lots.

Investigational medicinal product name	Pprevnar 13®
Investigational medicinal product code	
Other name	Pfizer Inc.'s Pneumococcal 13-valent conjugate vaccine (diphtheria CRM197 protein) (PCV-13)
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose administered IM in the anterolateral region of the left thigh at Visit 1 (Day 0), with either Inv_MMR vaccine or one of the two Com_MMR vaccine lots in US children only.

Arm title	COM_MMR
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Arm description:

Subjects received 1 dose of the licensed vaccine M-M-R®II or M-M-R Vax Pro™ Lot 1 or Lot 2 co administered with Varivax® and Havrix® vaccines at Day 0. Subjects recruited in the US also received Pprevnar 13® at Day 0.

Arm type	Active comparator
Investigational medicinal product name	M-M-R®II
Investigational medicinal product code	
Other name	M-M-R Vax Pro®
Pharmaceutical forms	Powder and solvent for suspension for injection in pre-filled syringe
Routes of administration	Subcutaneous use

Dosage and administration details:

1 dose administered SC in the tricep region of left arm.

Investigational medicinal product name	Havrix®
Investigational medicinal product code	SUB38555
Other name	Havrix junior 720 (GSK Biological Hepatitis A virus antigen (HAV))
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose administered intramuscularly (IM) in the anterolateral region of the right thigh at Visit 1 (Day 0), with either Inv_MMR vaccine or one of the two Com_MMR vaccine lots.

Investigational medicinal product name	Varivax®
Investigational medicinal product code	SUB25312
Other name	Merck & Co. Inc.'s Live attenuated Varicella
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose administered SC in the tricep region of right arm at Visit 1 (Day 0), with either Priorix® vaccine or one of the two M-M-R®II vaccine lots.

Investigational medicinal product name	Pprevnar 13®
Investigational medicinal product code	
Other name	Pfizer Inc.'s Pneumococcal 13-valent conjugate vaccine (diphtheria CRM197 protein) (PCV-13)
Pharmaceutical forms	Suspension for injection in pre-filled syringe
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose administered IM in the anterolateral region of the left thigh at Visit 1 (Day 0), with either Inv_MMR vaccine or one of the two Com_MMR vaccine lots in US children only.

Number of subjects in period 1^[2]	INV_MMR	COM_MMR
Started	1163	573
Completed	1116	543
Not completed	47	30
Consent withdrawn by subject	14	9
Loss Of Kaiser Insurance	1	-
2nd blooddraw & diary card incomplete	1	-
Traveling Outside The Country	1	-
Lost to follow-up	29	21
Family Out Of Country Until 9/29/2015	1	-

Notes:

[2] - 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: Out of 1743 subjects enrolled, 6 subjects with an allocated subject number did not receive the study vaccine dose and 1 subject was removed from the study.

Baseline characteristics

Reporting groups

Reporting group title	INV_MMR
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Reporting group description:

Subjects received 1 dose of the study vaccine Priorix® co administered with Varivax® and Havrix® vaccines at Day 0. Subjects recruited in the US also received Prevnar 13® at Day 0.

Reporting group title	COM_MMR
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Reporting group description:

Subjects received 1 dose of the licensed vaccine M-M-R®II or M-M-R Vax Pro™ Lot 1 or Lot 2 co administered with Varivax® and Havrix® vaccines at Day 0. Subjects recruited in the US also received Prevnar 13® at Day 0.

Reporting group values	INV_MMR	COM_MMR	Total
Number of subjects	1163	573	1736
Age categorical			
Units: Subjects			

Age continuous			
Age continuous description			
Units: months			
arithmetic mean	12.3	12.3	
standard deviation	± 0.7	± 0.7	-
Gender categorical			
Gender categorical description			
Units: Subjects			
Female	551	270	821
Male	612	303	915
Race/Ethnicity, Customized			
Units: Subjects			
African Heritage / African American	64	38	102
American Indian or Alaskan Native	29	16	45
Asian - Central/South Asian Heritage	8	5	13
Asian - East Asian Heritage	131	65	196
Asian - Japanese Heritage	2	0	2
Asian - South East Asian Heritage	28	12	40
Native Hawaiian or Other Pacific Islander	1	2	3
White - Arabic / North African Heritage	3	3	6
White - Caucasian / European Heritage	808	385	1193
Other	89	47	136

End points

End points reporting groups

Reporting group title	INV_MMR
Reporting group description: Subjects received 1 dose of the study vaccine Priorix® co administered with Varivax® and Havrix® vaccines at Day 0. Subjects recruited in the US also received Prevnar 13® at Day 0.	
Reporting group title	COM_MMR
Reporting group description: Subjects received 1 dose of the licensed vaccine M-M-R®II or M-M-R Vax Pro™ Lot 1 or Lot 2 co administered with Varivax® and Havrix® vaccines at Day 0. Subjects recruited in the US also received Prevnar 13® at Day 0.	

Primary: Number of subjects reporting fever after MMR (Priorix® or M-M-R®II) vaccination

End point title	Number of subjects reporting fever after MMR (Priorix® or M-M-R®II) vaccination
End point description: Fever was assessed for temperature equal to/above (\geq) 38°C and above ($>$) 39.0°C. The safety profile for fever was assessed based on the group difference (INV_MMR minus COM_MMR) in incidence of fever equal to or below the cut-off value.	
End point type	Primary
End point timeframe: During Day 5 to Day 12 post-vaccination period	

End point values	INV_MMR	COM_MMR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1125	556		
Units: Subjects				
≥ 38 °C	205	95		
> 39.0 °C	47	17		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: Null hypotheses: UL of the group difference (INV_MMR minus COM_MMR) in incidence of 95% CI is equal to or below (\leq) 10% for Fever ≥ 38 °C and equal to or below (\leq) 5% for Fever > 39.0 °C.	
Comparison groups	INV_MMR v COM_MMR

Number of subjects included in analysis	1681
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[1]
Parameter estimate	Difference in percentage between groups
Point estimate	1.14
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.84
upper limit	4.89

Notes:

[1] - Power obtained using PASS 2005 (Likelihood Score [Miettinen and Nurminen approach]), [Miettinen, 1985]), one-sided non-inferiority test for the difference of two independent proportions, under the alternative associated to the reference value & one-sided alpha=2.5%. The global power for these objectives was 90.3%

Statistical analysis title	Statistical analysis 2
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Statistical analysis description:

Null hypotheses: UL of the group difference (INV_MMR minus COM_MMR) in incidence of 95% CI is equal to or below (\leq) 10% for Fever $\geq 38^{\circ}\text{C}$ and equal to or below (\leq) 5% for Fever $> 39.0^{\circ}\text{C}$.

Comparison groups	INV_MMR v COM_MMR
Number of subjects included in analysis	1681
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[2]
Parameter estimate	Difference in percentage between groups
Point estimate	1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.92
upper limit	2.9

Notes:

[2] - Power obtained using PASS 2005 (Likelihood Score [Miettinen and Nurminen approach]), [Miettinen, 1985]), one-sided non-inferiority test for the difference of two independent proportions, under the alternative associated to the reference value & one-sided alpha=2.5%. The global power for these objectives was 90.3%.

Secondary: Number of subjects with anti-measles virus antibody concentration equal to or above the cut-off-value

End point title	Number of subjects with anti-measles virus antibody concentration equal to or above the cut-off-value
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End point description:

Seroresponse was defined as post-vaccination anti-measles virus antibody concentration ≥ 200 mIU/mL (ELISA, Enzygnost) among children who were seronegative (antibody concentration < 150 mIU/mL) before vaccination.

End point type	Secondary
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End point timeframe:

At Day 42 post vaccination

End point values	INV_MMR	COM_MMR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1042	522		
Units: subjects				
≥150 mIU/ml	1035	505		
≥200 mIU/ml	1032	504		

Statistical analyses

No statistical analyses for this end point

Secondary: Evaluation of immunogenicity in terms of anti-measles virus antibody concentrations

End point title	Evaluation of immunogenicity in terms of anti-measles virus antibody concentrations
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End point description:

Antibody concentrations are expressed as Geometric Mean Concentrations (GMCs) in mIU/mL. Analyses included initially seronegative subjects only.

End point type	Secondary
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End point timeframe:

At Day 42 post vaccination

End point values	INV_MMR	COM_MMR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1042	522		
Units: mIU/mL				
geometric mean (confidence interval 95%)	2751.2 (2617.6 to 2891.7)	3134 (2879.6 to 3410.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-mumps virus antibody concentration equal to or above the cut-off-value

End point title	Number of subjects with anti-mumps virus antibody concentration equal to or above the cut-off-value
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End point description:

For mumps virus, a seroresponse was defined as post-vaccination anti-mumps virus antibody concentration ≥ 10 EU/mL (ELISA, PPD) among children who were seronegative (antibody concentration < 5 EU/mL) before vaccination.

End point type	Secondary
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End point timeframe:

At Day 42 post vaccination

End point values	INV_MMR	COM_MMR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	963	484		
Units: Subjects				
≥5 EU/ml	961	481		
≥10 EU/ml	957	474		

Statistical analyses

No statistical analyses for this end point

Secondary: Evaluation of immunogenicity in terms of anti-mumps virus antibody concentrations

End point title	Evaluation of immunogenicity in terms of anti-mumps virus antibody concentrations
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End point description:

Antibody concentrations are expressed as Geometric Mean Concentrations (GMCs) in mIU/mL. Analyses included initially seronegative subjects only.

End point type	Secondary
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End point timeframe:

At Day 42 post vaccination

End point values	INV_MMR	COM_MMR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	963	484		
Units: mIU/mL				
geometric mean (confidence interval 95%)	86 (82 to 90.3)	82.6 (76.5 to 89.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-rubella virus antibody concentration equal to or above the cut-off-value

End point title	Number of subjects with anti-rubella virus antibody concentration equal to or above the cut-off-value
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End point description:

For rubella virus, a seroresponse was defined as post-vaccination anti-rubella virus antibody concentration ≥ 10 IU/mL (ELISA, Enzygnost) among children who were seronegative (antibody concentration < 4 IU/mL) before vaccination.

End point type	Secondary
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End point timeframe:

At Day 42 post vaccination

End point values	INV_MMR	COM_MMR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1042	522		
Units: subjects				
≥10 IU/ml	997	513		
≥4 IU/ml	1038	521		

Statistical analyses

No statistical analyses for this end point

Secondary: Evaluation of immunogenicity in terms of anti-rubella virus antibody concentrations

End point title	Evaluation of immunogenicity in terms of anti-rubella virus antibody concentrations
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End point description:

Antibody concentrations are expressed as Geometric Mean Concentrations (GMCs) in mIU/mL. Analyses included initially seronegative subjects only.

End point type	Secondary
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End point timeframe:

At Day 42 post vaccination

End point values	INV_MMR	COM_MMR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1042	522		
Units: mIU/mL				
geometric mean (confidence interval 95%)	45 (42.8 to 47.2)	66.8 (62.2 to 71.6)		

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
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End point description:

Assessed solicited local symptoms were pain, redness and swelling. Any = Occurrence of any local symptom regardless of their intensity grade. Grade 3 Pain = Cried when limb was moved/spontaneously painful.

End point type	Secondary
End point timeframe:	
During the 4-day (Days 0-3) post-vaccination period	

End point values	INV_MMR	COM_MMR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1122	554		
Units: Subjects				
Any pain	311	132		
Grade 3 pain	6	2		
Any redness	259	138		
Grade 3 redness (>20 mm)	7	8		
Any swelling	95	59		
Grade 3 swelling (>20 mm)	2	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with solicited general symptoms

End point title	Number of subjects with solicited general symptoms
End point description:	
Assessed solicited general symptoms were Drowsiness, Irritability/fussiness, and loss of appetite. Any= occurrence of any general symptom regardless of intensity grade or relationship to vaccination, Grade 3 drowsiness = symptom that prevented normal activity, Grade 3 irritability/fussiness =crying that could not be comforted/ symptom that prevented normal activity, Grade 3 loss of appetite = did not eat at all.	
End point type	Secondary
End point timeframe:	
During the 15-day (Days 0-14) post-vaccination period	

End point values	INV_MMR	COM_MMR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1125	556		
Units: Subjects				
Any drowsiness	526	239		
Grade 3 drowsiness	31	13		
Any irritability/fussiness	721	346		
Grade 3 irritability/fussiness	41	20		
Any loss of appetite	492	233		
Grade 3 loss of appetite	20	10		

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:

End point type | Secondary

End point timeframe:

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

End point values	INV_MMR	COM_MMR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1125	556		
Units: Subjects				
≥38 °C	349	180		
>39.5 °C	45	15		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting MMR specific solicited general symptoms

End point title | Number of subjects reporting MMR specific solicited general symptoms

End point description:

Assessed MMR specific symptoms were parotid gland swelling and any suspected signs of meningism including febrile convulsions. Any = occurrence of any general symptom regardless of intensity grade or relationship to vaccination, Grade 3 Febrile convulsion = Prevented everyday activity, Grade 3 Parotid gland = Swelling with accompanied general symptoms, Related = event assessed by the investigator as causally related to the study vaccination.

End point type | Secondary

End point timeframe:

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

End point values	INV_MMR	COM_MMR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1125	556		
Units: Subjects				
Any febrile convulsion	2	0		
Grade 3 febrile convulsion	1	0		
Related febrile convulsion	1	0		
Any parotid gland swelling	0	0		

Grade 3 parotid gland swelling	0	0		
Related parotid gland swelling	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting investigator-confirmed rash

End point title	Number of subjects reporting investigator-confirmed rash
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End point description:

Assessed any rash, Grade 3, Related, Localized rash, Generalized rash, measles/rubella-rash. Grade 3 Measles/rubella/varicella-like rash = Rash with more than150 lesions .Other Grade 3 Rash = Rash that prevented normal, everyday activities. Related = Rash assessed by the investigator as causally related to study vaccination.

End point type	Secondary
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End point timeframe:

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

End point values	INV_MMR	COM_MMR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1125	556		
Units: Subjects				
Any localized or generalized	274	153		
Any with fever	99	49		
Any varicella like	39	23		
Any measles/rubella like	65	26		
Any grade 3	22	8		
Any related	70	37		
Localized any	185	98		
Localized administration site	8	4		
Localized other site	177	96		
Localized with fever	53	26		
Localized varicella like	26	14		
Localized measles/rubella like	22	12		
Localized grade 3	2	1		
Localized related	24	21		
Generalized any	108	65		
Generalized with fever	48	25		
Generalized varicella like	13	9		
Generalized measles/rubella like	45	16		
Generalized grade 3	20	7		
Generalized related	47	20		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting unsolicited adverse events

End point title | Number of subjects reporting unsolicited adverse events

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-day (Days 0-42) post-vaccination period

End point values	INV_MMR	COM_MMR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1163	573		
Units: Subjects	597	278		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting new onset chronic diseases (NOCDs)

End point title | Number of subjects reporting new onset chronic diseases (NOCDs)

End point description:

End point type | Secondary

End point timeframe:

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

End point values	INV_MMR	COM_MMR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1163	573		
Units: Subjects	29	11		

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	COM_MMR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1163	573		
Units: Subjects	166	55		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting AEs leading to a medically attended visit

End point title	Number of subjects reporting AEs leading to a medically attended visit
End point description: An event for which the child received medical attention defined as hospitalization, an emergency room visit or a visit to or from medical personnel (e.g., nurse practitioner or physician assistant or medical doctor) for any reason.	
End point type	Secondary
End point timeframe: Day 0 through the end of the study (Day 180)	

End point values	INV_MMR	COM_MMR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1163	573		
Units: Subjects	717	319		

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 resulted in death, was life-threatening, required hospitalization or prolongation of existing hospitalization or resulted 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	COM_MMR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1163	573		
Units: Subjects	24	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting measles-like illness

End point title	Number of subjects reporting measles-like illness
End point description:	
Measles-like illness was defined as the occurrence of the following signs and symptoms in the absence of another confirmed diagnosis: maculopapular rash, fever ($\geq 38^{\circ}\text{C}$), and at least one symptom of cough, coryza, conjunctivitis, or diarrhea, with fever or rash occurring between Day 5 and Day 12 inclusive. Other event must be one of cough, coryza, conjunctivitis, or diarrhea.	
End point type	Secondary
End point timeframe:	
Between Day 5 and Day 12 (inclusive) post-vaccination	

End point values	INV_MMR	COM_MMR		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1163	573		
Units: Subjects				
Measles-like illness	18	5		
Maculopapular rash plus fever and one other event	26	9		
Maculopapular rash and fever	89	44		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

Serious Adverse events (SAE) = Entire study period (180 days).

Adverse event reporting additional description:

The frequent adverse event data is currently being re-analyzed and the record will be updated once it becomes available.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	18.1
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Reporting groups

Reporting group title	INV_MMR Group
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Reporting group description:

Subjects received 1 dose of the study vaccine Priorix® co administered with Varivax® and Havrix® vaccines at Day 0. Subjects recruited in the US also received Prevnar 13® at Day 0.

Reporting group title	COM_MMR Group
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Reporting group description:

Subjects received 1 dose of the licensed vaccine M-M-R®II or M-M-R Vax Pro™ Lot 1 or Lot 2 co administered with Varivax® and Havrix® vaccines at Day 0. Subjects recruited in the US also received Prevnar 13® at Day 0.

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: The frequent adverse event data is currently being re-analyzed and the record will be updated once it becomes available.

Serious adverse events	INV_MMR Group	COM_MMR Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	24 / 1163 (2.06%)	9 / 573 (1.57%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Limb injury			
subjects affected / exposed	1 / 1163 (0.09%)	0 / 573 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	1 / 1163 (0.09%)	0 / 573 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lethargy			

subjects affected / exposed	1 / 1163 (0.09%)	0 / 573 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	1 / 1163 (0.09%)	0 / 573 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Immune thrombocytopenic purpura			
subjects affected / exposed	0 / 1163 (0.00%)	1 / 573 (0.17%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	1 / 1163 (0.09%)	0 / 573 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastritis			
subjects affected / exposed	0 / 1163 (0.00%)	1 / 573 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Bronchial hyperreactivity			
subjects affected / exposed	0 / 1163 (0.00%)	1 / 573 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive airways disorder			
subjects affected / exposed	1 / 1163 (0.09%)	0 / 573 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	1 / 1163 (0.09%)	1 / 573 (0.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Musculoskeletal and connective tissue disorders			
Joint effusion			
subjects affected / exposed	1 / 1163 (0.09%)	0 / 573 (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			
Acute sinusitis			
subjects affected / exposed	1 / 1163 (0.09%)	0 / 573 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial infection			
subjects affected / exposed	0 / 1163 (0.00%)	1 / 573 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			
subjects affected / exposed	1 / 1163 (0.09%)	1 / 573 (0.17%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 1163 (0.09%)	2 / 573 (0.35%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 1163 (0.09%)	0 / 573 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Croup infectious			
subjects affected / exposed	1 / 1163 (0.09%)	0 / 573 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Exanthema subitum			
subjects affected / exposed	1 / 1163 (0.09%)	0 / 573 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Fungal skin infection			
subjects affected / exposed	0 / 1163 (0.00%)	1 / 573 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 1163 (0.09%)	0 / 573 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis norovirus			
subjects affected / exposed	1 / 1163 (0.09%)	0 / 573 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis salmonella			
subjects affected / exposed	1 / 1163 (0.09%)	0 / 573 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	1 / 1163 (0.09%)	0 / 573 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand-foot-and-mouth disease			
subjects affected / exposed	1 / 1163 (0.09%)	0 / 573 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 1163 (0.00%)	1 / 573 (0.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngitis			
subjects affected / exposed	1 / 1163 (0.09%)	0 / 573 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			

subjects affected / exposed	1 / 1163 (0.09%)	0 / 573 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Parainfluenzae virus infection		
subjects affected / exposed	1 / 1163 (0.09%)	0 / 573 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Periorbital cellulitis		
subjects affected / exposed	1 / 1163 (0.09%)	0 / 573 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pneumonia		
subjects affected / exposed	4 / 1163 (0.34%)	1 / 573 (0.17%)
occurrences causally related to treatment / all	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Pneumonia respiratory syncytial viral		
subjects affected / exposed	1 / 1163 (0.09%)	0 / 573 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Respiratory syncytial virus infection		
subjects affected / exposed	1 / 1163 (0.09%)	0 / 573 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Salmonellosis		
subjects affected / exposed	1 / 1163 (0.09%)	0 / 573 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Staphylococcal infection		
subjects affected / exposed	1 / 1163 (0.09%)	0 / 573 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Tonsillitis		

subjects affected / exposed	1 / 1163 (0.09%)	0 / 573 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 1163 (0.09%)	0 / 573 (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			
Dehydration			
subjects affected / exposed	3 / 1163 (0.26%)	0 / 573 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	1 / 1163 (0.09%)	0 / 573 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemia			
subjects affected / exposed	1 / 1163 (0.09%)	0 / 573 (0.00%)	
occurrences causally related to treatment / all	0 / 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	INV_MMR Group	COM_MMR Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 1163 (0.00%)	0 / 573 (0.00%)	

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