Clinical trial results:
A phase IIIb, open label, randomized, multicenter study of the immunogenicity and safety of a booster dose of Kinrix when co-administered with varicella vaccine (Varivax®, Merck and Company) and MMR vaccine (M-M-R®II, Merck and Company), compared to that of a booster dose of Kinrix co-administered with MMR vaccine only, in healthy children 4 to 6 years of age.

Summary

EudraCT number	2011-002946-11
Trial protocol	Outside EU/EEA
Global end of trial date	15 June 2010

Results information

Result version number	v3 (current)
This version publication date	16 September 2018
First version publication date	05 July 2015
Version creation reason	• Correction of full data set Minor corrections of the full study results.

Trial information

Trial identification

Sponsor protocol code	111852

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00871117
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	24 September 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 January 2010
Global end of trial reached?	Yes
Global end of trial date	15 June 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the non-inferiority of Kinrix co-administered with Varivax and M-M-RII compared to Kinrix co-administered with M-M-RII only in terms of diphtheria (D), tetanus (T), pertussis (PT), filamentous hemagglutinin (FHA), and pertactin (PRN) booster response and poliovirus geaometric mean titres (GMTs), one month after vaccination with Kinrix.

Protection of trial subjects:

All subjects were supervised closely for at least 30 minutes following vaccination with appropriate medical treatment readily available. Vaccines were administered by qualified and trained personnel. Vaccines were administered only to eligible subjects that had no contraindications to any components of the vaccines. Subjects were followed-up from the time the subject consents to participate in the study until she/he is discharged.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 March 2009
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	United States: 478
Worldwide total number of subjects	478
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	478

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:

478 subjects were enrolled, but 2 subjects who received a subject number were not vaccinated. Therefore the total amount of subjects used for the analysis was 476.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Kinrix + M-M-R II + Varivax

Arm description:

Subjects received at Day 0 one dose of Kinrix, intramuscularly in the deltoid region of the left upper arm, co-administered with one dose of M-M-R II and Varivax each, subcutaneously in the deltoid of the right upper and lower arm, respectively.

Arm type	Experimental
Investigational medicinal product name	GSK Biologicals'Kinrix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose administered intramuscularly in the deltoid region of the left upper arm at Day 0

Investigational medicinal product name	Merck and Company's M-M-R II
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

One dose administered subcutaneously in the deltoid of the right upper arm at Day 0

Investigational medicinal product name	Merck and Company's Varivax
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

One dose at Day 0 administered subcutaneously in the deltoid region of the right lower arm

Arm title	Kinrix + M-M-R II -> Varivax

Arm description:

Subjects received at Day 0 one dose of Kinrix, intramuscularly in the deltoid region of the left upper arm, co-administered with one dose of M-M-R II, subcutaneously in the deltoid of the right upper arm. At Day 30 they received one dose of Varivax subcutaneously in the deltoid region of the right upper arm.

Arm type	Active comparator

Investigational medicinal product name	GSK Biologicals'Kinrix
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose administered intramuscularly in the deltoid region of the left upper arm at Day 0

Investigational medicinal product name	Merck and Company's M-M-R II
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

One dose administered subcutaneously in the deltoid of the right upper arm at Day 0

Investigational medicinal product name	Merck and Company's Varivax
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

One dose administered subcutaneously in the deltoid region of the right lower arm at Day 30

Number of subjects in period 1[1]	Kinrix + M-M-R II + Varivax	Kinrix + M-M-R II -> Varivax
Started	239	237
Completed	234	227
Not completed	5	10
Others	-	4
Lost to follow-up	5	6

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: 478 subjects were enrolled, but 2 subjects who received a subject number were not vaccinated. Therefore the total amount of subjects used for the analysis was 476.

Baseline characteristics

Reporting groups	
Reporting group title	Kinrix + M-M-R II + Varivax
Reporting group description:	
Subjects received at Day 0 one dose of Kinrix, intramuscularly in the deltoid region of the left upper arm, co-administered with one dose of M-M-R II and Varivax each, subcutaneously in the deltoid of the right upper and lower arm, respectively.	
Reporting group title	Kinrix + M-M-R II -> Varivax
Reporting group description:	
Subjects received at Day 0 one dose of Kinrix, intramuscularly in the deltoid region of the left upper arm, co-administered with one dose of M-M-R II, subcutaneously in the deltoid of the right upper arm. At Day 30 they received one dose of Varivax subcutaneously in the deltoid region of the right upper arm.	

Reporting group values	Kinrix + M-M-R II + Varivax	Kinrix + M-M-R II -> Varivax	Total
Number of subjects	239	237	476
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: years			
arithmetic mean	4.2	4.2	
standard deviation	± 0.41	± 0.37	-
Gender categorical			
Units: Subjects			
Female	129	123	252
Male	110	114	224
Race/Ethnicity			
Units: Subjects			
African heritage/African American	27	23	50
American Indian or Alaskan Native	35	33	68
Asian-Central/South Asian heritage	7	11	18
Asian-East Asian heritage	3	5	8
Asian-South East Asian heritage	13	17	30
Native Hawaiian or Other Pacific Islander	2	3	5
White-Arabic/North African heritage	1	6	7
White-Caucasian/European heritage	109	107	216
Unspecified	42	32	74

End points

End points reporting groups

Reporting group title	Kinrix + M-M-R II + Varivax

Reporting group description:

Subjects received at Day 0 one dose of Kinrix, intramuscularly in the deltoid region of the left upper arm, co-administered with one dose of M-M-R II and Varivax each, subcutaneously in the deltoid of the right upper and lower arm, respectively.

Reporting group title	Kinrix + M-M-R II -> Varivax

Reporting group description:

Subjects received at Day 0 one dose of Kinrix, intramuscularly in the deltoid region of the left upper arm, co-administered with one dose of M-M-R II, subcutaneously in the deltoid of the right upper arm. At Day 30 they received one dose of Varivax subcutaneously in the deltoid region of the right upper arm.

Primary: Number of subjects with booster responses to diphteria and tetanus

End point title	Number of subjects with booster responses to diphteria and tetanus

End point description:

Anti-diphteria (anti-D) and anti-tetanus (anti-T) booster response was defined as: - initially seronegative subjects (sero-) (pre-booster antibody concentration below cut-off of < 0.1 international units per milliliter (IU/mL)) with an increase of at least four times the cut-off one month after vaccination (post-booster antibody concentration ≥0.4 IU/mL) - initially seropositive subjects (sero+) (pre-booster antibody concentration ≥0.1 IU/mL) with an increase of at least four times the pre-booster antibody concentration one month after vaccination.

End point type	Primary

End point timeframe:

One month after Kinrix vaccination (Month 1), prior to Varivax vaccination for Kinrix + M-M-R II -> Varivax Group.

End point values	Kinrix + M-M-R II + Varivax	Kinrix + M-M-R II -> Varivax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	211	209		
Units: Subjects				
Anti-D (N=211;209)	209	207		
Anti-T (N=211;208)	208	203		

Statistical analyses

Statistical analysis title	Difference in booster response rates for anti-D

Statistical analysis description:

To demonstrate the non-inferiority of DTaP-IPV vaccine co-administered with Varicella and MMR vaccines compared to DTaP-IPV vaccine co-administered with MMR only in terms of diphtheria (D) booster response one month after vaccination with DTaP-IPV vaccine.

Comparison groups	Kinrix + M-M-R II + Varivax v Kinrix + M-M-R II -> Varivax

Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Parameter estimate	Difference in booster response rates
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.54
upper limit	2.58

Notes:

[1] - Lower limit of the standardized asymptotic 95% confidence interval (CI) for the between-group differences in booster response to diphtheria was greater than or equal to (≥)-10%.

Statistical analysis title	Difference in booster response rates for anti-T

Statistical analysis description:

To demonstrate the non-inferiority of DTaP-IPV vaccine co-administered with Varicella and MMR vaccines compared to DTaP-IPV vaccine co-administered with MMR only in terms of tetanus (T) booster response one month after vaccination with DTaP-IPV vaccine.

Comparison groups	Kinrix + M-M-R II + Varivax v Kinrix + M-M-R II -> Varivax
Number of subjects included in analysis	420
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Parameter estimate	Difference in booster response rates
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.99
upper limit	4.26

Notes:

[2] - Lower limit of the standardized asymptotic 95% CI for the between-group differences in booster response to tetanus was ≥ -10%.

Primary: Number of subjects with anti-pertussis toxoid (anti-PT), anti-filamentous hemagglutinin (FHA) and anti-pertactin (anti-PRN) booster responses, measured in Enzyme-Linked Immunosorbent Assay Units per milliliter (EL.U/mL)

End point title	Number of subjects with anti-pertussis toxoid (anti-PT), anti-filamentous hemagglutinin (FHA) and anti-pertactin (anti-PRN) booster responses, measured in Enzyme-Linked Immunosorbent Assay Units per milliliter (EL.U/mL)

End point description:

Anti-PT, anti-FHA and anti-PRN booster response : - initially sero- (pre-booster antibody concentration below cut-off < 5.0 EL.U/mL) with increase of at least four times cut-off one month after vaccination (concentration post-booster ≥20.0 EL.U/mL) - initially sero+ with pre-booster antibody concentration ≥5.0 EL.U/mL and < 20.0 EL.U/mL with increase of at least four times pre-booster concentration one month post-booster - initially sero+ with pre-booster antibody concentration ≥20.0 EL.U/mL with an increase of at least two times the pre-booster antibody concentration one month post-booster

End point type	Primary

End point timeframe:

One month after Kinrix vaccination (Month 1), prior to Varivax vaccination for Kinrix + M-M-R II -> Varivax Group.

End point values	Kinrix + M-M-R II + Varivax	Kinrix + M-M-R II -> Varivax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	220	212		
Units: Subjects				
Anti-PT (N=218;210)	207	201		
Anti-FHA (N=216;210)	213	209		
Anti-PRN (N=220;212)	220	209		

Statistical analyses

Statistical analysis title	Difference in vaccine response rates for anti-PT

Statistical analysis description:

To demonstrate the non-inferiority of DTaP-IPV vaccine co-administered with Varicella and MMR vaccines compared to DTaP-IPV vaccine co-administered with MMR only in terms of pertussis toxoid (PT) booster response one month after vaccination with DTaP-IPV vaccine.

Comparison groups	Kinrix + M-M-R II + Varivax v Kinrix + M-M-R II -> Varivax
Number of subjects included in analysis	432
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Difference in booster response rates
Point estimate	-0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.07
upper limit	3.51

Notes:

[3] - Lower limit of the standardized asymptotic 95% CI for the between-group differences in booster response to PT was ≥ -10%.

Statistical analysis title	Difference in vaccine response rates for anti-FHA

Statistical analysis description:

To demonstrate the non-inferiority of DTaP-IPV vaccine co-administered with Varicella and MMR vaccines compared to DTaP-IPV vaccine co-administered with MMR only in terms of filamentous hemagglutinin (FHA) booster response one month after vaccination with DTaP-IPV vaccine.

Comparison groups	Kinrix + M-M-R II + Varivax v Kinrix + M-M-R II -> Varivax
Number of subjects included in analysis	432
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Parameter estimate	Difference in booster response rates
Point estimate	-0.91

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.59
upper limit	1.39

Notes:

[4] - Lower limit of the standardized asymptotic 95% CI for the between-group differences in booster response to FHA was ≥ -10%.

Statistical analysis title	Difference in vaccine response rates for anti-PRN

Statistical analysis description:

To demonstrate the non-inferiority of DTaP-IPV vaccine co-administered with Varicella and MMR vaccines compared to DTaP-IPV vaccine co-administered with MMR only in terms of pertactin (PRN) booster response one month after vaccination with DTaP-IPV vaccine.

Comparison groups	Kinrix + M-M-R II + Varivax v Kinrix + M-M-R II -> Varivax
Number of subjects included in analysis	432
Analysis specification	Pre-specified
Analysis type	non-inferiority[5]
Parameter estimate	Difference in booster response rates
Point estimate	1.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.32
upper limit	4.08

Notes:

[5] - Lower limit of the standardized asymptotic 95% CI for the between-group differences in booster response to PRN, was ≥ -10%.

Primary: Geometric Mean Titers (GMTs) for antibodies to poliovirus types 1, 2 and 3

End point title	Geometric Mean Titers (GMTs) for antibodies to poliovirus types 1, 2 and 3

End point description:

Titers are expressed as GMTs.

End point type	Primary

End point timeframe:

One month after Kinrix vaccination (Month 1), prior to Varivax vaccination for Kinrix + M-M-R II -> Varivax Group.

End point values	Kinrix + M-M-R II + Varivax	Kinrix + M-M-R II -> Varivax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	219	212		
Units: Titer				
geometric mean (confidence interval 95%)				
Anti-Polio 1 (N=219;211)	1638.4 (1441 to 1863)	1789.9 (1559 to 2054.9)		
Anti-Polio 2 (N=218;212)	1572.9 (1387.8 to 1782.7)	1902.6 (1678.6 to 2156.5)		

Anti-Polio 3 (N=219;212)	2588.4 (2282.7 to 2935)	3189.6 (2798.2 to 3635.7)		

Statistical analyses

Statistical analysis title	Adjusted GMT ratio for anti-Polio1

Statistical analysis description:

To demonstrate the non-inferiority of DTaP-IPV vaccine co-administered with Varicella and MMR vaccines compared to DTaP-IPV vaccine co-administered with MMR only in terms of poliovirus type 1 geometric mean titers (GMTs), one month after vaccination with DTaP-IPV vaccine.

Comparison groups	Kinrix + M-M-R II + Varivax v Kinrix + M-M-R II -> Varivax
Number of subjects included in analysis	431
Analysis specification	Pre-specified
Analysis type	non-inferiority[6]
Parameter estimate	Adjusted GMT ratio
Point estimate	0.91
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1.1

Notes:

[6] - Lower limit of the 95% CI for the GMT ratios for poliovirus type 1 antigens was ≥0.67

Statistical analysis title	Adjusted GMT ratio for anti-Polio2

Statistical analysis description:

To demonstrate the non-inferiority of DTaP-IPV vaccine co-administered with Varicella and MMR vaccines compared to DTaP-IPV vaccine co-administered with MMR only in terms of poliovirus type 2 geometric mean titers (GMTs), one month after vaccination with DTaP-IPV vaccine.

Comparison groups	Kinrix + M-M-R II + Varivax v Kinrix + M-M-R II -> Varivax
Number of subjects included in analysis	431
Analysis specification	Pre-specified
Analysis type	non-inferiority[7]
Parameter estimate	Adjusted GMT ratio
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	0.99

Notes:

[7] - Lower limit of the 95% CI for the GMT ratios of poliovirus type 2 antigens was ≥0.67

Statistical analysis title	Adjusted GMT ratio for anti-Polio3

Statistical analysis description:

To demonstrate the non-inferiority of DTaP-IPV vaccine co-administered with Varicella and MMR vaccines compared to DTaP-IPV vaccine co-administered with MMR only in terms of poliovirus type 3

geometric mean titers (GMTs), one month after vaccination with DTaP-IPV vaccine.

Comparison groups	Kinrix + M-M-R II + Varivax v Kinrix + M-M-R II -> Varivax
Number of subjects included in analysis	431
Analysis specification	Pre-specified
Analysis type	non-inferiority[8]
Parameter estimate	Adjusted GMT ratio
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	1.01

Notes:

[8] - Lower limit of the 95% CI for the GMT ratios of poliovirus type 3 antigens was ≥0.67

Secondary: Number of subjects with anti-D and anti-T antibody concentrations above cut-off value

End point title	Number of subjects with anti-D and anti-T antibody concentrations above cut-off value

End point description:

Cut-off value was defined as greater than or equal to 1.0 international units per milliliter (IU/mL).

End point type	Secondary

End point timeframe:

One month after Kinrix vaccination (Month 1), prior to Varivax vaccination for Kinrix + M-M-R II -> Varivax Group.

End point values	Kinrix + M-M-R II + Varivax	Kinrix + M-M-R II -> Varivax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	217	212		
Units: Subjects				
Anti-D	217	212		
Anti-T	217	209		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Concentrations (GMCs) for anti-D and anti-T antibodies

End point title	Geometric Mean Concentrations (GMCs) for anti-D and anti-T antibodies

End point description:

Concentrations were expressed as GMCs in IU/mL.

End point type	Secondary

End point timeframe:

One month after Kinrix vaccination (Month 1), prior to Varivax vaccination for Kinrix + M-M-R II -> Varivax Group.

End point values	Kinrix + M-M-R II + Varivax	Kinrix + M-M-R II -> Varivax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	217	212		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-D	14.273 (12.989 to 15.684)	14.809 (13.397 to 16.371)		
Anti-T	8.658 (7.888 to 9.504)	8.138 (7.323 to 9.045)		

Statistical analyses

No statistical analyses for this end point

Secondary: GMCs for anti-PT, anti-FHA, anti-PRN antibodies

End point title	GMCs for anti-PT, anti-FHA, anti-PRN antibodies

End point description:

Concentrations are expressed as GMCs in Enzyme-Linked Immunosorbent Assay (ELISA) Units per milliliter (EL.U/mL).

End point type	Secondary

End point timeframe:

One month after Kinrix vaccination (Month 1), prior to Varivax vaccination for Kinrix + M-M-R II -> Varivax Group.

End point values	Kinrix + M-M-R II + Varivax	Kinrix + M-M-R II -> Varivax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	220	212		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PT	96.5 (85.8 to 108.6)	101.3 (89.2 to 115.1)		
Anti-FHA	968.9 (886.9 to 1058.4)	968.2 (876 to 1070.1)		
Anti-PRN	627.1 (543.2 to 724)	620.4 (530.3 to 725.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with an anti-polio 1, 2, 3 booster response

End point title	Number of subjects with an anti-polio 1, 2, 3 booster response

End point description:

Anti-poliovirus 1, anti-poliovirus 2 and anti-poliovirus 3 booster response: - initially seronegative subjects (pre-booster antibody titer below cut-off of 8 ED50) with an antibody titer ≥ 32 ED50 one month after vaccination - initially seropositive subjects (pre-booster antibody titers ≥ 8 ED50) with an increase at least four times the pre-booster antibody titer one month after vaccination. ED50 is defined here as the reverse of the dilution resulting in 50% inhibition. The lowest dilution at which serum samples were tested is 1:8 from which a test was considered positive.

End point type	Secondary

End point timeframe:

One month after Kinrix vaccination (Month 1), prior to Varivax vaccination for Kinrix + M-M-R II -> Varivax Group.

End point values	Kinrix + M-M-R II + Varivax	Kinrix + M-M-R II -> Varivax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	215	211		
Units: Subjects				
Anti-polio 1 (N=215;209)	211	202		
Anti-polio 2 (N=214;211)	204	207		
Anti-polio 3 (N=215;211)	213	207		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroprotected against diphteria and tetanus

End point title	Number of subjects seroprotected against diphteria and tetanus

End point description:

Seroprotection status was defined as: * anti-D antibody concentration greater than or equal to 0.1 IU/mL * anti-T antibody concentration greater than or equal to 0.1 IU/mL

End point type	Secondary

End point timeframe:

One month after Kinrix vaccination (Month 1), prior to Varivax vaccination for Kinrix + M-M-R II -> Varivax Group.

End point values	Kinrix + M-M-R II + Varivax	Kinrix + M-M-R II -> Varivax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	217	212		
Units: Subjects				
Anti-D	217	212		
Anti-T	217	212		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroprotected against poliovirus 1, 2 and 3

End point title	Number of subjects seroprotected against poliovirus 1, 2 and 3

End point description:

Seroprotection was defined: * anti-poliovirus type 1, 2 or 3 antibody titer greater than or equal to 8 ED50. ED50 is defined here as the reverse of the dilution resulting in 50% inhibition.

End point type	Secondary

End point timeframe:

One month after Kinrix vaccination (Month 1), prior to Varivax vaccination for Kinrix + M-M-R II -> Varivax Group.

End point values	Kinrix + M-M-R II + Varivax	Kinrix + M-M-R II -> Varivax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	219	212		
Units: Subjects				
Anti-Polio 1 (N=219;211)	219	211		
Anti-Polio 2 (N=218;212)	218	212		
Anti-Polio 3 (N=219;212)	219	212		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seropositive for anti-PT, anti-FHA and anti-PRN antibodies

End point title	Number of subjects seropositive for anti-PT, anti-FHA and anti-PRN antibodies

End point description:

Seropositivity was defined as a concentration greater than or equal to 5.0 EL.U/mL

End point type	Secondary

End point timeframe:

One month after Kinrix vaccination (Month 1), prior to Varivax vaccination for Kinrix + M-M-R II -> Varivax Group.

End point values	Kinrix + M-M-R II + Varivax	Kinrix + M-M-R II -> Varivax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	220	212		
Units: Subjects				
anti-PT	220	212		
anti-FHA	220	212		
anti-PRN	220	212		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any solicited local symptoms

End point title	Number of subjects with any solicited local symptoms

End point description:

Solicited local symptoms included pain, redness and swelling at the injection site. Any was defined as incidence of a particular symptom regardless of intensity grade.

End point type	Secondary

End point timeframe:

Within 4 days (Day 0 to 3) after booster immunization * for Kinrix + M-M-R II -> Varivax Group before vaccination with Varivax

End point values	Kinrix + M-M-R II + Varivax	Kinrix + M-M-R II -> Varivax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	230	230		
Units: Subjects				
Any Pain	156	166		
Any Redness	115	114		
Any Swelling	95	84		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with unsolicited adverse events

End point title	Number of subjects with unsolicited adverse events

End point description:

An unsolicited adverse event is any adverse event (i.e. any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product) 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 will be reported as an unsolicited adverse event.

End point type	Secondary

End point timeframe:

Up to 31 days (Day 0 through Day 30) after booster vaccination * for Kinrix + M-M-R II -> Varivax Group before vaccination with Varivax

End point values	Kinrix + M-M-R II + Varivax	Kinrix + M-M-R II -> Varivax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239	237		
Units: Subjects				
Number of subjects with unsolicited adverse events	75	72		

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 are medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization, result in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subject.

End point type	Secondary

End point timeframe:

During the entire study period (from Day 0 to 6 months post-vaccination)

End point values	Kinrix + M-M-R II + Varivax	Kinrix + M-M-R II -> Varivax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239	237		
Units: Subjects				
Number of subjects with serious adverse events (SA	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any solicited general symptoms

End point title	Number of subjects with any solicited general symptoms

End point description:

Solicited general symptoms included fever [temperature equal to or greater than 37.5 degrees Celsius (°C)], drowsiness and loss of appetite. Any was defined as incidence of a particular symptom regardless of intensity grade.

End point type	Secondary

End point timeframe:

Within 4 days (Day 0 to 3) after booster immunization * for Kinrix + M-M-R II -> Varivax Group before vaccination with Varivax

End point values	Kinrix + M-M-R II + Varivax	Kinrix + M-M-R II -> Varivax		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	230	230		
Units: Subjects				
Any Drowsiness	61	66		
Any Loss of appetite	60	57		
Any Temperature (Axillary)	58	68		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited local/general Adverse Events (AEs) during the first 4 days (Day 0-3) post vaccination ; unsolicited AEs during the 31 days (Days 0-30) post vaccination and SAEs during the entire study period (from Day 0 to 6 months post-vaccination).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13.0

Reporting groups

Reporting group title	Kinrix + M-M-R II -> Varivax

Reporting group description:

Subjects received at Day 0 one dose of Kinrix,intramuscularly in the deltoid region of the left upper arm, co-administered with one dose of M-M-R II, subcutaneously in the deltoid of the right upper arm. At Day 30 they received one dose of Varivax subcutaneously in the deltoid region of the right upper arm.

Reporting group title	Kinrix + M-M-R II + Varivax

Reporting group description:

Subjects received at Day 0 one dose of Kinrix,intramuscularly in the deltoid region of the left upper arm, co-administered with one dose of M-M-R II, subcutaneously in the deltoid of the right upper arm, and one dose of Varivax subcutaneously in the deltoid region of the right lower arm.

Serious adverse events	Kinrix + M-M-R II -> Varivax	Kinrix + M-M-R II + Varivax	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 237 (0.42%)	0 / 239 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Infections and infestations			
Croup infectious			
subjects affected / exposed	1 / 237 (0.42%)	0 / 239 (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	Kinrix + M-M-R II -> Varivax	Kinrix + M-M-R II + Varivax	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	230 / 237 (97.05%)	228 / 239 (95.40%)	
General disorders and administration site conditions			

Pain			
subjects affected / exposed[1]	166 / 230 (72.17%)	156 / 230 (67.83%)	
occurrences (all)	166	156	
Redness			
subjects affected / exposed[2]	114 / 230 (49.57%)	115 / 230 (50.00%)	
occurrences (all)	114	115	
Swelling			
subjects affected / exposed[3]	84 / 230 (36.52%)	95 / 230 (41.30%)	
occurrences (all)	84	95	
Drowsiness			
subjects affected / exposed[4]	66 / 230 (28.70%)	61 / 230 (26.52%)	
occurrences (all)	66	61	
Loss of appetite			
subjects affected / exposed[5]	57 / 230 (24.78%)	60 / 230 (26.09%)	
occurrences (all)	57	60	
Fever			
subjects affected / exposed[6]	68 / 230 (29.57%)	58 / 230 (25.22%)	
occurrences (all)	68	58	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This solicited local symptom was only collected from subjects with their symptom sheets completed.

[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This solicited local symptom was only collected from subjects with their symptom sheets completed.

[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This solicited local symptom was only collected from subjects with their symptom sheets completed.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This solicited general symptom was only collected from subjects with their symptom sheets completed.

[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This solicited general symptom was only collected from subjects with their symptom sheets completed.

[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This solicited general symptom was only collected from subjects with their symptom sheets completed.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 January 2009	Both Kinrix and the second dose of Varivax are indicated in children 4-6 years of age, and there is great potential for the vaccines to be given concurrently. To date there are no data examining the concurrent administration of Kinrix and Varivax. The aim of this trial is to demonstrate that co-administered Varivax does not negatively affect the immunogenicity or reactogenicity of Kinrix.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported