



Clinical trial results:

A Phase III, double blind, randomized, comparative study of the safety and immunogenicity of GSK Biologicals' Varilrix HSA-free varicella vaccine and Varilrix™ given as a 2 dose course in the second year of life
Summary

EudraCT number	2013-003535-30
Trial protocol	DE GB EE
Global end of trial date	17 February 2017

Results information

Result version number	v1 (current)
This version publication date	28 May 2017
First version publication date	28 May 2017

Trial information

Trial identification

Sponsor protocol code	200147
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02570126
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, (44)2089 904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, (44)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	25 October 2016
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	17 February 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate the safety profile (i.e. fever above (>) 39°C (> 102.2°F)) of Varilrix HSA-free compared to Varilrix™ post Dose 1

Criterion:

For the Varilrix HSA-free vaccine as compared to Varilrix™, the upper limit (UL) of the 2-sided standardised asymptotic 95% confidence interval (CI) for the group difference (VAR_HSA_F minus VAR) in incidence of fever > 39.0°C (> 102.2°F) within 0-14 days after Dose 1 is equal to or below 5%

Protection of trial subjects:

All subjects were observed closely for at least 30 minutes following the administration of vaccine, with appropriate medical treatment readily available in case of an anaphylactic reaction

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 November 2015
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: 164
Country: Number of subjects enrolled	Germany: 237
Country: Number of subjects enrolled	Mexico: 142
Country: Number of subjects enrolled	Thailand: 265
Country: Number of subjects enrolled	United Kingdom: 423
Worldwide total number of subjects	1231
EEA total number of subjects	824

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)	1229
Children (2-11 years)	2

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: -

Pre-assignment period milestones

Number of subjects started	1231
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Number of subjects completed	1231
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Period 1

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

The laboratory in charge of the laboratory testing was blinded to the treatment, and codes were used to link the subject and study (without any link to the treatment attributed to the subject) to each sample

Arms

Are arms mutually exclusive?	Yes
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Arm title	VAR_HSA_F Group
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Arm description:

2 doses of Varilrix HSA-free vaccine, one at Visit 1 (Day 0) and the other at Visit 2 (Day 42), were given to the subjects in this group. The vaccine was administered subcutaneously in the triceps region of the left arm

Arm type	Experimental
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Investigational medicinal product name	Varilrix HSA-free
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Powder and solvent for solution for injection
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Routes of administration	Subcutaneous use
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Dosage and administration details:

2 doses administered, one at Day 0 and the other at Day 42

Arm title	VAR Group
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Arm description:

2 doses of Varilrix™ vaccine, one at Visit 1 (Day 0) and the other at Visit 2 (Day 42), were given to the subjects in this group. The vaccine was administered subcutaneously in the triceps region of the left arm

Arm type	Active comparator
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Investigational medicinal product name	Varilrix™
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Powder and solvent for solution for injection
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Routes of administration	Subcutaneous use
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Dosage and administration details:

2 doses administered, one at Day 0 and the other at Day 42

Number of subjects in period 1	VAR_HSA_F Group	VAR Group
Started	615	616
Completed	609	607
Not completed	6	9
Consent withdrawn by subject	3	7
Violation of Procedures GSK	-	1
Unable to Arrange Visit 3	1	-
Lost to follow-up	2	-
Protocol deviation	-	1

Baseline characteristics

Reporting groups

Reporting group title	VAR_HSA_F Group
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Reporting group description:

2 doses of Varilrix HSA-free vaccine, one at Visit 1 (Day 0) and the other at Visit 2 (Day 42), were given to the subjects in this group. The vaccine was administered subcutaneously in the triceps region of the left arm

Reporting group title	VAR Group
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Reporting group description:

2 doses of Varilrix™ vaccine, one at Visit 1 (Day 0) and the other at Visit 2 (Day 42), were given to the subjects in this group. The vaccine was administered subcutaneously in the triceps region of the left arm

Reporting group values	VAR_HSA_F Group	VAR Group	Total
Number of subjects	615	616	1231
Age categorical			
Units: Subjects			

Age continuous			
Units: months			
arithmetic mean	16.7	16.9	
standard deviation	± 3.3	± 3.4	-
Gender categorical			
Units: Subjects			
Female	318	312	630
Male	297	304	601
Race/Ethnicity, Customized			
Units: Subjects			
African Heritage / African American	3	1	4
Asian - Central/South Asian Heritage	2	2	4
Asian - East Asian Heritage	3	2	5
Asian - South East Asian Heritage	133	135	268
Other	94	94	188
White - Arabic / North African Heritage	1	1	2
White - Caucasian / European Heritage	379	381	760

End points

End points reporting groups

Reporting group title	VAR_HSA_F Group
Reporting group description: 2 doses of Varilrix HSA-free vaccine, one at Visit 1 (Day 0) and the other at Visit 2 (Day 42), were given to the subjects in this group. The vaccine was administered subcutaneously in the triceps region of the left arm	
Reporting group title	VAR Group
Reporting group description: 2 doses of Varilrix™ vaccine, one at Visit 1 (Day 0) and the other at Visit 2 (Day 42), were given to the subjects in this group. The vaccine was administered subcutaneously in the triceps region of the left arm	

Primary: Number of subjects reporting fever

End point title	Number of subjects reporting fever
End point description: Fever was defined as axillary temperature above (>) 39.0 °C (> 102.2°F)	
End point type	Primary
End point timeframe: 15-days (Days 0-14) post Dose 1 of varicella vaccination	

End point values	VAR_HSA_F Group	VAR Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	612	614		
Units: Subjects				
Subjects	24	32		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Statistical analysis description: For the Varilrix HSA-free as compared to Varilrix™, the upper limit (UL) of the 2-sided standardised asymptotic 95% confidence interval (CI) for the group difference (VAR_HSA_F minus VAR) in incidence of fever >39.0°C (>102.2°F) within 0-14 days after Dose 1 was to be equal to or below 5%	
Comparison groups	VAR Group v VAR_HSA_F Group
Number of subjects included in analysis	1226
Analysis specification	Pre-specified
Analysis type	non-inferiority ^[1]
Parameter estimate	Difference in percentage between groups
Point estimate	-1.29

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.72
upper limit	1.08

Notes:

[1] - Non-inferiority of Varilrix HSA-free vaccine to Varilrix™ vaccine in terms of percentage of subjects reporting fever >39.0°C (>102.2°F) within 15-days (Days 0-14) after Dose 1 (VAR_HSA_F Group minus VAR Group).

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

Secondary: Number of subjects reporting fever

End point title	Number of subjects reporting fever
End point description:	
Fever was defined as axillary temperature greater than or equal to (\geq) 38.0°C (\geq 100.4°F)	
End point type	Secondary
End point timeframe:	
15 days post each dose of varicella vaccination	

End point values	VAR_HSA_F Group	VAR Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	612	614		
Units: Subjects				
Fever \geq 38 °C following Dose 1	83	92		
Fever \geq 38 °C following Dose 2	83	86		

Statistical analyses

No statistical analyses for this end point

Secondary: Evaluation of immune response to varicella vaccine with respect to Anti Varicella Zoster Virus (Anti-VZV) antibody concentrations (immuno-sub cohort)

End point title	Evaluation of immune response to varicella vaccine with respect to Anti Varicella Zoster Virus (Anti-VZV) antibody concentrations (immuno-sub cohort)
End point description:	
Anti-VZY antibody concentrations were expressed in terms of Geometric Mean Concentrations (GMCs)	
End point type	Secondary
End point timeframe:	
At Day 42 and Day 84 post vaccination	

End point values	VAR_HSA_F Group	VAR Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	185	173		
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Post Dose 1 blood sample at Day 42	139.9 (126.7 to 154.5)	146 (132.5 to 160.7)		
Post Dose 2 blood sample at Day 84	931.8 (841.1 to 1032.3)	1102.4 (996.1 to 1220.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with a seroresponse to VZV (immuno sub cohort)

End point title	Number of subjects with a seroresponse to VZV (immuno sub cohort)
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End point description:

For VZV, seroresponse was defined as, post-vaccination anti-VZV antibody concentration \geq 50 mIU/mL among subjects who were seronegative (antibody concentration below ($<$) 25 mIU/mL) before vaccination

End point type	Secondary
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End point timeframe:

At Day 42 and Day 84 post vaccination

End point values	VAR_HSA_F Group	VAR Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	185	173		
Units: Subjects				
\geq 25 mIU/mL (At Day 42)	184	168		
\geq 50 mIU/mL (At Day 42)	174	166		
\geq 25 mIU/mL (At Day 84)	180	173		
\geq 50 mIU/mL (At Day 84)	180	173		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting solicited local symptoms

End point title	Number of subjects reporting solicited local symptoms
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End point description:

Solicited local symptoms assessed were pain, injection site redness and swelling. Any = occurrence of the specified solicited local symptom regardless of its intensity. Grade 3 pain = subject crying when limb was moved or as spontaneously painful. Grade 3 redness and swelling = above ($>$) 20 mm

End point type	Secondary
End point timeframe:	
4-day post vaccination period following Dose 1 (Day 0) and Dose 2 (Day 42)	

End point values	VAR_HSA_F Group	VAR Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	612	614		
Units: Subjects				
Any Pain, Dose 1	75	86		
Grade 3 Pain, Dose 1	2	4		
Any Redness, Dose 1	149	150		
Grade 3 Redness, Dose 1	3	2		
Any Swelling, Dose 1	43	42		
Grade 3 Swelling, Dose 1	2	1		
Any Pain, Dose 2	63	80		
Grade 3 Pain, Dose 2	1	1		
Any Redness, Dose 2	168	185		
Grade 3 Redness, Dose 2	10	8		
Any Swelling, Dose 2	69	71		
Grade 3 Swelling, Dose 2	1	4		
Any Pain, Across Doses	101	126		
Grade 3 Pain, Across Doses	3	5		
Any Redness, Across Doses	224	234		
Grade 3 Redness, Across Doses	13	10		
Any Swelling, Across Doses	92	94		
Grade 3 Swelling, Across Doses	3	4		

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:	
Any fever ($\geq 38^{\circ}\text{C}$) = occurrence of any fever regardless of its intensity grade or relationship to vaccination. Grade 3 fever = temperature $> 39.5^{\circ}\text{C}$. Related fever = assessed by the investigator as causally related to study vaccination	
End point type	Secondary
End point timeframe:	
43-day post vaccination period following Dose 1 (Day 0) and Dose 2 (Day 42)	

End point values	VAR_HSA_F Group	VAR Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	612	614		
Units: Subjects				
Fever (Axillary), Dose 1 : $\geq 38^{\circ}\text{C}$	205	188		
Fever (Axillary), Dose 1 : $> 39.5^{\circ}\text{C}$	40	27		
Fever (Axillary), Dose 1 : Related	72	51		
Fever (Axillary), Dose 2 : $\geq 38^{\circ}\text{C}$	172	177		
Fever (Axillary), Dose 2 : $> 39.5^{\circ}\text{C}$	23	31		
Fever (Axillary), Dose 2 : Related	51	57		
Fever (Axillary), Across Doses : $\geq 38^{\circ}\text{C}$	301	290		
Fever (Axillary), Across Doses : $> 39.5^{\circ}\text{C}$	57	53		
Fever (Axillary), Across Doses : Related	111	95		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting rash

End point title	Number of subjects reporting rash
End point description:	
Any rash = occurrence of the specified solicited general symptom regardless of its intensity. Grade 3 rash = rash which prevented normal, everyday activities. Related rash = assessed by the investigator as causally related to study vaccination	
End point type	Secondary
End point timeframe:	
43-day post vaccination period following Dose 1 (Day 0) and Dose 2 (Day 42)	

End point values	VAR_HSA_F Group	VAR Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	612	614		
Units: Subjects				
Any, Dose 1 : Localised or generalised	89	104		
Any, Dose 1 : With fever	32	27		
Any, Dose 1 : Varicella like	7	9		
Any, Dose 1 : Grade 3	2	4		
Any, Dose 1 : Related	16	23		
Localised, Dose 1 : Any	65	74		
Localised, Dose 1 : Administration site	4	2		
Localised, Dose 1 : Other site	63	72		
Localised, Dose 1 : With fever	18	12		
Localised, Dose 1 : Varicella like	5	4		
Localised, Dose 1 : Grade 3	2	1		
Localised, Dose 1 : Related	11	13		
Generalised, Dose 1 : Any	29	35		

Generalised, Dose 1 : With fever	14	15		
Generalised, Dose 1 : Varicella like	2	6		
Generalised, Dose 1 : Grade 3	0	3		
Generalised, Dose 1 : Related	5	11		
Any, Dose 2 : Localised or generalised	76	78		
Any, Dose 2 : With fever	27	34		
Any, Dose 2 : Varicella like	4	5		
Any, Dose 2 : Grade 3	2	5		
Any, Dose 2 : Related	15	16		
Localised, Dose 2 : Any	52	57		
Localised, Dose 2 : Administration site	1	4		
Localised, Dose 2 : Other site	51	53		
Localised, Dose 2 : With fever	16	23		
Localised, Dose 2 : Varicella like	3	2		
Localised, Dose 2 : Grade 3	1	1		
Localised, Dose 2 : Related	12	9		
Generalised, Dose 2 : Any	25	26		
Generalised, Dose 2 : With fever	11	12		
Generalised, Dose 2 : Varicella like	1	3		
Generalised, Dose 2 : Grade 3	1	4		
Generalised, Dose 2 : Related	3	8		
Any, Across Doses : Localised or generalised	144	152		
Any, Across Doses : With fever	55	59		
Any, Across Doses : Varicella like	11	14		
Any, Across Doses : Grade 3	4	9		
Any, Across Doses : Related	28	37		
Localised, Across Doses : Any	106	112		
Localised, Across Doses : Administration site	5	6		
Localised, Across Doses : Other site	103	107		
Localised, Across Doses : With fever	32	34		
Localised, Across Doses : Varicella like	8	6		
Localised, Across Doses : Grade 3	3	2		
Localised, Across Doses : Related	20	21		
Generalised, Across Doses : Any	49	57		
Generalised, Across Doses : With fever	24	27		
Generalised, Across Doses : Varicella like	3	9		
Generalised, Across Doses : Grade 3	1	7		
Generalised, Across Doses : Related	8	19		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting febrile convulsions

End point title	Number of subjects reporting febrile convulsions
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End point description:

Any febrile convulsion = occurrence of the specified solicited general symptom regardless of its

intensity. Grade 3 febrile convulsion = febrile convulsion which prevented normal, everyday activities.
Related febrile convulsion = assessed by the investigator as causally related to study vaccination

End point type	Secondary
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End point timeframe:

43-day post vaccination period following Dose 1 (Day 0) and Dose 2 (Day 42)

End point values	VAR_HSA_F Group	VAR Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	612	614		
Units: Subjects				
Febrile convulsion, Dose 1 : Any	1	1		
Febrile convulsion, Dose 1 : Grade 3	0	1		
Febrile convulsion, Dose 1 : Related	0	0		
Febrile convulsion, Dose 2 : Any	0	1		
Febrile convulsion, Dose 2 : Grade 3	0	0		
Febrile convulsion, Dose 2 : Related	0	0		
Febrile convulsion, Across Doses : Any	1	2		
Febrile convulsion, Across Doses : Grade 3	0	1		
Febrile convulsion, Across Doses : Related	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting unsolicited adverse events (AEs)

End point title	Number of subjects reporting unsolicited adverse events (AEs)
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End point description:

Unsolicited AE covers any AE reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any = occurrence of any unsolicited symptom regardless of intensity grade or relation to vaccination

End point type	Secondary
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End point timeframe:

43-day post vaccination period following Dose 1 (Day 0) and Dose 2 (Day 42)

End point values	VAR_HSA_F Group	VAR Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	615	616		
Units: Subjects				
Post Dose 1	270	282		
Post Dose 2	223	220		

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)
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End point description:

SAEs assessed included medical occurrences that resulted in death, were life threatening, required hospitalisation or prolongation of hospitalisation or resulted in disability/incapacity. Any SAE = occurrence of SAE regardless of intensity grade or relation to vaccination

End point type	Secondary
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End point timeframe:

From Day 0 through the end of study (Day 84)

End point values	VAR_HSA_F Group	VAR Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	615	616		
Units: Subjects				
Subjects	13	15		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited local AEs: During the 4-day post vaccination period after each dose. Solicited general and unsolicited AEs: During the 43-day post vaccination period after each dose. Serious adverse events: From Day 0 through the end of study (Day 84)

Adverse event reporting additional description:

For the systematically assessed other (non-serious) adverse events, the number of participants at risk included those from Total Vaccinated Cohort who had the symptom sheet completed

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	19.1
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Reporting groups

Reporting group title	VAR_HSA_F Group
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Reporting group description:

2 doses of Varilrix HSA-free vaccine, one at Visit 1 (Day 0) and the other at Visit 2 (Day 42), were given to the subjects in this group. The vaccine was administered subcutaneously in the triceps region of the left arm

Reporting group title	VAR Group
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Reporting group description:

2 doses of Varilrix™ vaccine, one at Visit 1 (Day 0) and the other at Visit 2 (Day 42), were given to the subjects in this group. The vaccine was administered subcutaneously in the triceps region of the left arm

Serious adverse events	VAR_HSA_F Group	VAR Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 615 (2.11%)	15 / 616 (2.44%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Congenital, familial and genetic disorders			
Hydrocele			
subjects affected / exposed	0 / 615 (0.00%)	1 / 616 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	1 / 615 (0.16%)	1 / 616 (0.16%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			

Pyrexia			
subjects affected / exposed	1 / 615 (0.16%)	0 / 616 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 615 (0.00%)	1 / 616 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Food poisoning			
subjects affected / exposed	0 / 615 (0.00%)	1 / 616 (0.16%)	
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			
Asthmatic crisis			
subjects affected / exposed	1 / 615 (0.16%)	0 / 616 (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			
Bronchitis			
subjects affected / exposed	1 / 615 (0.16%)	1 / 616 (0.16%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Croup infectious			
subjects affected / exposed	0 / 615 (0.00%)	1 / 616 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear infection			
subjects affected / exposed	0 / 615 (0.00%)	1 / 616 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand-foot-and-mouth disease			

subjects affected / exposed	1 / 615 (0.16%)	0 / 616 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpangina			
subjects affected / exposed	0 / 615 (0.00%)	1 / 616 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 615 (0.00%)	1 / 616 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasopharyngitis			
subjects affected / exposed	1 / 615 (0.16%)	0 / 616 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media acute			
subjects affected / exposed	0 / 615 (0.00%)	1 / 616 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
subjects affected / exposed	1 / 615 (0.16%)	0 / 616 (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	6 / 615 (0.98%)	3 / 616 (0.49%)	
occurrences causally related to treatment / all	0 / 7	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			
subjects affected / exposed	0 / 615 (0.00%)	1 / 616 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudocroup			

subjects affected / exposed	0 / 615 (0.00%)	1 / 616 (0.16%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 615 (0.16%)	0 / 616 (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 / 615 (0.16%)	0 / 616 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	1 / 615 (0.16%)	0 / 616 (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	VAR_HSA_F Group	VAR Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	489 / 615 (79.51%)	491 / 616 (79.71%)	
General disorders and administration site conditions			
Injection site erythema			
subjects affected / exposed	224 / 615 (36.42%)	237 / 616 (38.47%)	
occurrences (all)	319	341	
Injection site swelling			
subjects affected / exposed	92 / 615 (14.96%)	95 / 616 (15.42%)	
occurrences (all)	112	114	
Injection site pain			
subjects affected / exposed	101 / 615 (16.42%)	127 / 616 (20.62%)	
occurrences (all)	138	167	
Pyrexia			
subjects affected / exposed	301 / 615 (48.94%)	290 / 616 (47.08%)	
occurrences (all)	377	365	

Gastrointestinal disorders	Diarrhoea			
	subjects affected / exposed	38 / 615 (6.18%)	39 / 616 (6.33%)	
	occurrences (all)	44	53	
	Teething			
	subjects affected / exposed	58 / 615 (9.43%)	55 / 616 (8.93%)	
	occurrences (all)	130	80	
Vomiting	subjects affected / exposed	31 / 615 (5.04%)	34 / 616 (5.52%)	
	occurrences (all)	34	39	
Respiratory, thoracic and mediastinal disorders				
Cough	subjects affected / exposed	57 / 615 (9.27%)	49 / 616 (7.95%)	
	occurrences (all)	71	59	
Skin and subcutaneous tissue disorders				
Rash	subjects affected / exposed	144 / 615 (23.41%)	152 / 616 (24.68%)	
	occurrences (all)	165	182	
Infections and infestations				
Nasopharyngitis	subjects affected / exposed	87 / 615 (14.15%)	80 / 616 (12.99%)	
	occurrences (all)	110	102	
Rhinitis	subjects affected / exposed	33 / 615 (5.37%)	25 / 616 (4.06%)	
	occurrences (all)	40	32	
Upper respiratory tract infection	subjects affected / exposed	28 / 615 (4.55%)	37 / 616 (6.01%)	
	occurrences (all)	35	42	

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