Clinical trial results:
An Open-Label, Multicenter, Single-arm Study to Evaluate the Immunogenicity of VARIVAX™ in Healthy Russian Individuals 12 Months of Age and Older

Summary

EudraCT number	2019-003903-36
Trial protocol	Outside EU/EEA
Global end of trial date	19 June 2020

Results information

Result version number	v2 (current)
This version publication date	12 March 2021
First version publication date	20 December 2020
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	V210-058

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03843632
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.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	19 June 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 June 2020
Global end of trial reached?	Yes
Global end of trial date	19 June 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The purpose of this study was to evaluate the immunogenicity of VARIVAX™ vaccine in healthy Russian children, adolescents, and adults. No formal hypothesis was tested.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 March 2019
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	Russian Federation: 150
Worldwide total number of subjects	150
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)	64
Adolescents (12-17 years)	36
Adults (18-64 years)	50
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study enrolled healthy Russians aged 12 months and older. Additional inclusion criteria applied.

Pre-assignment

Screening details:

150 participants were enrolled and received VARIVAX™ on study. Adults and Adolescents received 2 vaccinations on study and children received 1 vaccination.

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	VARIVAX Adults (18 to 75 years)

Arm description:

Participants aged 18 to 75 years of age received 2 doses of VARIVAX™ administered approximately six weeks apart: one 0.5 mL dose of VARIVAX™ administered by subcutaneous (SC) injection on Day 1, and a second 0.5 mL dose of VARIVAX™ by SC injection on Day 43.

Arm type	Experimental
Investigational medicinal product name	VARIVAX™
Investigational medicinal product code	
Other name	Varicella Virus Vaccine Live
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

All participants received one 0.5 mL dose of VARIVAX™ administered by SC injection on Day 1. Adult participants and adolescent participants 13 to 17 years of age also received a second 0.5 mL dose of VARIVAX™ by SC injection on Day 43.

Arm title	VARIVAX™ Adolescents 13 to 17 years of age

Arm description:

Participants aged 13 to 17 years of age received 2 doses of VARIVAX™ administered approximately six weeks apart: one 0.5 mL dose of VARIVAX™ administered by SC injection on Day 1, and a second 0.5 mL dose of VARIVAX™ by SC injection on Day 43.

Arm type	Experimental
Investigational medicinal product name	VARIVAX™
Investigational medicinal product code	
Other name	Varicella Virus Vaccine Live
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

All participants received one 0.5 mL dose of VARIVAX™ administered by SC injection on Day 1. Adult participants and adolescent participants 13 to 17 years of age also received a second 0.5 mL dose of VARIVAX™ by SC injection on Day 43.

Arm title	VARIVAX™ Children 7 to 12 years of age

Arm description:

Participants aged 7 to 12 years of age received one 0.5 mL dose of VARIVAX™ administered by SC injection on Day 1.

Arm type	Experimental

Investigational medicinal product name	VARIVAX
Investigational medicinal product code	
Other name	Varicella Virus Vaccine Live
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

All participants received one 0.5 mL dose of VARIVAX™ administered by SC injection on Day 1.

Arm title	VARIVAX™ Children 12 months to 6 years of age

Arm description:

Participants aged 12 months to 6 years of age received one 0.5 mL dose of VARIVAX™ administered by SC injection on Day 1.

Arm type	Experimental
Investigational medicinal product name	VARIVAX
Investigational medicinal product code	
Other name	Varicella Virus Vaccine Live
Pharmaceutical forms	Suspension for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

All participants received one 0.5 mL dose of VARIVAX™ administered by SC injection on Day 1.

Number of subjects in period 1	VARIVAX Adults (18 to 75 years)	VARIVAX™ Adolescents 13 to 17 years of age	VARIVAX™ Children 7 to 12 years of age
Started	50	30	33
Vaccination 1	50	30	33
Vaccination 2	49	30	0 [1]
Completed	49	30	33
Not completed	1	0	0
Consent withdrawn by subject	1	-	-

Number of subjects in period 1	VARIVAX™ Children 12 months to 6 years of age
Started	37
Vaccination 1	37
Vaccination 2	0 [2]
Completed	37
Not completed	0
Consent withdrawn by subject	-

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Only adults and adolescents 13 to 17 years of age received Vaccination 2.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.
Justification: Only adults and adolescents 13 to 17 years of age received Vaccination 2.

Baseline characteristics

Reporting groups	
Reporting group title	VARIVAX Adults (18 to 75 years)
Reporting group description:	
Participants aged 18 to 75 years of age received 2 doses of VARIVAX™ administered approximately six weeks apart: one 0.5 mL dose of VARIVAX™ administered by subcutaneous (SC) injection on Day 1, and a second 0.5 mL dose of VARIVAX™ by SC injection on Day 43.	
Reporting group title	VARIVAX™ Adolescents 13 to 17 years of age
Reporting group description:	
Participants aged 13 to 17 years of age received 2 doses of VARIVAX™ administered approximately six weeks apart: one 0.5 mL dose of VARIVAX™ administered by SC injection on Day 1, and a second 0.5 mL dose of VARIVAX™ by SC injection on Day 43.	
Reporting group title	VARIVAX™ Children 7 to 12 years of age
Reporting group description:	
Participants aged 7 to 12 years of age received one 0.5 mL dose of VARIVAX™ administered by SC injection on Day 1.	
Reporting group title	VARIVAX™ Children 12 months to 6 years of age
Reporting group description:	
Participants aged 12 months to 6 years of age received one 0.5 mL dose of VARIVAX™ administered by SC injection on Day 1.	

Reporting group values	VARIVAX Adults (18 to 75 years)	VARIVAX™ Adolescents 13 to 17 years of age	VARIVAX™ Children 7 to 12 years of age
Number of subjects	50	30	33
Age Categorical Units: Participants			
Age Continuous Units: years			
arithmetic mean	24.7	15.1	9.6
standard deviation	± 6.0	± 1.5	± 1.6
Gender Categorical Units: Participants			
Female	36	16	14
Male	14	14	19
Race Units: Subjects			
White	50	30	33
Ethnicity Units: Subjects			
Hispanic Or Latino	1	0	0
Not Hispanic Or Latino	48	30	33
Not Reported	1	0	0
Serostatus for Varicella-Zoster Virus (VZV) Units: Subjects			
VZV Seronegative	26	18	22
VZV Seropositive	24	12	11

Reporting group values	VARIVAX™ Children	Total	

	12 months to 6 years of age		
Number of subjects	37	150	
Age Categorical Units: Participants			
Age Continuous Units: years			
arithmetic mean	3.2		
standard deviation	± 1.6	-	
Gender Categorical Units: Participants			
Female	18	84	
Male	19	66	
Race Units: Subjects			
White	37	150	
Ethnicity Units: Subjects			
Hispanic Or Latino	0	1	
Not Hispanic Or Latino	37	148	
Not Reported	0	1	
Serostatus for Varicella-Zoster Virus (VZV) Units: Subjects			
VZV Seronegative	34	100	
VZV Seropositive	3	50	

End points

End points reporting groups

Reporting group title	VARIVAX Adults (18 to 75 years)
Reporting group description:	
Participants aged 18 to 75 years of age received 2 doses of VARIVAX™ administered approximately six weeks apart: one 0.5 mL dose of VARIVAX™ administered by subcutaneous (SC) injection on Day 1, and a second 0.5 mL dose of VARIVAX™ by SC injection on Day 43.	
Reporting group title	VARIVAX™ Adolescents 13 to 17 years of age
Reporting group description:	
Participants aged 13 to 17 years of age received 2 doses of VARIVAX™ administered approximately six weeks apart: one 0.5 mL dose of VARIVAX™ administered by SC injection on Day 1, and a second 0.5 mL dose of VARIVAX™ by SC injection on Day 43.	
Reporting group title	VARIVAX™ Children 7 to 12 years of age
Reporting group description:	
Participants aged 7 to 12 years of age received one 0.5 mL dose of VARIVAX™ administered by SC injection on Day 1.	
Reporting group title	VARIVAX™ Children 12 months to 6 years of age
Reporting group description:	
Participants aged 12 months to 6 years of age received one 0.5 mL dose of VARIVAX™ administered by SC injection on Day 1.	

Primary: Varicella Zoster Virus (VZV) Antibody Response Rate at 6 Weeks Post Last Vaccination in Participants Who Were Seronegative at Baseline

End point title	Varicella Zoster Virus (VZV) Antibody Response Rate at 6 Weeks Post Last Vaccination in Participants Who Were Seronegative at Baseline[1]
End point description:	
VZV antibody titers were measured using a glycoprotein enzyme-linked immunosorbent assay (gpELISA). The VZV antibody response rate was defined as the percentage of participants with a post-vaccination VZV antibody titer ≥5 gpELISA units/mL for participants whose baseline VZV antibody titer was <1.25 gpELISA units/mL. VZV antibody response rate was reported for all study arms at 6 weeks post last vaccination (Vaccination 1 for children and Vaccination 2 for adults and adolescents) for participants who were seronegative to VZW at baseline. All allocated participants without deviations from the protocol that would substantially affect the results of the immunogenicity outcome measures (Per-Protocol population) who were seronegative at baseline and who received Vaccination 1 (children) or Vaccination 1 and Vaccination 2 (adults and adolescents) were analyzed.	
End point type	Primary
End point timeframe:	
Adults and Adolescents: 6 weeks post Vaccination 2 (up to approximately 86 days), Children: 6 weeks post Vaccination 1 (up to approximately 43 days)	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no between-group statistical analyses for this endpoint.

End point values	VARIVAX Adults (18 to 75 years)	VARIVAX™ Adolescents 13 to 17 years of age	VARIVAX™ Children 7 to 12 years of age	VARIVAX™ Children 12 months to 6 years of age
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	18	22	34
Units: Percentage of participants				
number (confidence interval 95%)	100 (86.8 to 100.0)	100 (81.5 to 100.0)	95.5 (77.2 to 99.9)	100.0 (89.7 to 100.0)

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titers (GMTs) of VZV Antibodies at 6 Weeks Post Last Vaccination in Participants Who Were Seronegative at Baseline

End point title	Geometric Mean Titers (GMTs) of VZV Antibodies at 6 Weeks Post Last Vaccination in Participants Who Were Seronegative at Baseline[2]

End point description:

GMTs of VZV antibodies were measured post-vaccination using a gpELISA. GMT was calculated at each time point by taking the log of the titers, averaging over all participants values, and then back-transforming to the original scale. GMT was reported for all study arms at 6 weeks post last vaccination (Vaccination 1 for children and Vaccination 2 for adults and adolescents) for participants who were seronegative to VZW at baseline. All allocated participants without deviations from the protocol that would substantially affect the results of the immunogenicity outcome measures (Per-Protocol population) who were seronegative at baseline and who received Vaccination 1 (children) or Vaccination 1 and Vaccination 2 (adults and adolescents) were analyzed.

End point type	Primary

End point timeframe:

Adults and Adolescents: 6 weeks post Vaccination 2 (up to approximately 86 days), Children: 6 weeks post Vaccination 1 (up to approximately 43 days)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no between-group statistical analyses for this endpoint.

End point values	VARIVAX Adults (18 to 75 years)	VARIVAX™ Adolescents 13 to 17 years of age	VARIVAX™ Children 7 to 12 years of age	VARIVAX™ Children 12 months to 6 years of age
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	18	22	34
Units: gpELISA units/mL				
geometric mean (confidence interval 95%)	70.7 (47.9 to 104.2)	78.6 (46.5 to 133.0)	11.3 (7.3 to 17.5)	13.9 (11.2 to 17.2)

Statistical analyses

No statistical analyses for this end point

Primary: VZV Antibody Seroconversion Rate at 6 Weeks Post Last Vaccination in Participants Who Were Seronegative at Baseline

End point title	VZV Antibody Seroconversion Rate at 6 Weeks Post Last Vaccination in Participants Who Were Seronegative at Baseline[3]

End point description:

VZV antibody levels were measured using a gpELISA. The VZW antibody seroconversion rate was

defined as the percentage of participants with VZV antibodies ≥1.25 gpELISA units/mL in participants with a baseline VZV antibody titer <1.25 gpELISA units/mL. VZW antibody seroconversion was reported for all study arms at 6 weeks post last vaccination (Vaccination 1 for children and Vaccination 2 for adults and adolescents) for participants who were seronegative to VZW at baseline. All allocated participants without deviations from the protocol that would substantially affect the results of the immunogenicity outcome measures (Per-Protocol population) who were seronegative at baseline and who received Vaccination 1 (children) or Vaccination 1 and Vaccination 2 (adults and adolescents) were analyzed.

End point type	Primary

End point timeframe:

Adults and Adolescents: 6 weeks post Vaccination 2 (up to approximately 86 days), Children: 6 weeks post Vaccination 1 (up to approximately 43 days)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no between-group statistical analyses for this endpoint.

End point values	VARIVAX Adults (18 to 75 years)	VARIVAX™ Adolescents 13 to 17 years of age	VARIVAX™ Children 7 to 12 years of age	VARIVAX™ Children 12 months to 6 years of age
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	26	18	22	34
Units: Percentage of participants				
number (confidence interval 95%)	100.0 (86.8 to 100.0)	100.0 (81.5 to 100.0)	95.5 (77.2 to 99.9)	100.0 (89.7 to 100.0)

Statistical analyses

No statistical analyses for this end point

Primary: GMTs of VZV Antibodies at Day 1 and 6 Weeks Post Last Vaccination in Participants Who Were Seropositive at Baseline

End point title	GMTs of VZV Antibodies at Day 1 and 6 Weeks Post Last Vaccination in Participants Who Were Seropositive at Baseline[4]

End point description:

GMTs of VZV antibodies were measured post-vaccination using a gpELISA. GMT was calculated at each time point by taking the log of the titers, averaging over all participants values, and then back-transforming to the original scale. GMT was reported for all study arms at 6 weeks post last vaccination (Vaccination 1 for children and Vaccination 2 for adults and adolescents) for participants who were seropositive to VZW at baseline. Confidence intervals (CIs) were only calculated when there were at least 5 participants who were seropositive in a treatment group; missing CIs indicated by "9999". All allocated participants without deviations from the protocol that would substantially affect the results of the immunogenicity outcome measures (Per-Protocol population) who were seropositive at baseline and who received Vaccination 1 (children) or Vaccination 1 and Vaccination 2 (adults and adolescents) were analyzed.

End point type	Primary

End point timeframe:

Day 1 (Baseline), 6 weeks post last vaccination (Day 43 for children and Day 84 for adults and adolescents)

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no between-group statistical analyses for this endpoint.

End point values	VARIVAX Adults (18 to 75 years)	VARIVAX™ Adolescents 13 to 17 years of age	VARIVAX™ Children 7 to 12 years of age	VARIVAX™ Children 12 months to 6 years of age
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23	12	11	3
Units: gpELISA units/mL				
geometric mean (confidence interval 95%)				
Day 1 (Baseline)	71.1 (31.4 to 161.2)	13.4 (5.8 to 31.0)	24.8 (7.2 to 85.5)	4.2 (-9999 to 9999)
Post Last Vaccination	216.7 (132.8 to 353.6)	151.7 (92.5 to 248.6)	125.0 (37.9 to 411.7)	47.6 (-9999 to 9999)

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Fold Rise (GMFR) in VZV Antibody Titers From Day 1 to 6 Weeks Post Last Vaccination in Participants Who Were Seropositive at Baseline

End point title	Geometric Mean Fold Rise (GMFR) in VZV Antibody Titers From Day 1 to 6 Weeks Post Last Vaccination in Participants Who Were Seropositive at Baseline[5]

End point description:

GMTs were measured using a gpELISA. For participants who were seropositive at baseline (baseline VZV antibody titer ≥1.25 gpELISA units/mL), the GMFR was calculated as the ratio of the VZV GMT at 6 weeks post last vaccination to the VZV GMT at Day 1 (baseline). The GMFR from Day 1 was reported for all study arms at 6 weeks post last vaccination (Vaccination 1 for children and Vaccination 2 for adults and adolescents) for participants who were seropositive to VZW at baseline. CIs were only calculated when there were at least 5 participants who were seropositive in a treatment group; missing CIs indicated by "9999". All allocated participants without deviations from the protocol that would substantially affect the results of the immunogenicity outcome measures (Per-Protocol population) who were seropositive at baseline and who received Vaccination 1 (children) or Vaccination 1 and Vaccination 2 (adults and adolescents) were analyzed.

End point type	Primary

End point timeframe:

Day 1 (Baseline), 6 weeks post last vaccination (Day 43 for children and Day 84 for adults and adolescents)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no between-group statistical analyses for this endpoint.

End point values	VARIVAX Adults (18 to 75 years)	VARIVAX™ Adolescents 13 to 17 years of age	VARIVAX™ Children 7 to 12 years of age	VARIVAX™ Children 12 months to 6 years of age
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23	12	11	3
Units: Ratio				
geometric mean (confidence interval 95%)	3.0 (2.0 to 4.8)	11.3 (4.6 to 27.5)	5.0 (2.6 to 9.7)	11.2 (-9999 to 9999)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Participants With ≥4-Fold Rise in Antibody Titers From Day 1 to 6 Weeks Post Last Vaccination Among Participants Who Were Seropositive at Baseline

End point title	Percentage of Participants With ≥4-Fold Rise in Antibody Titers From Day 1 to 6 Weeks Post Last Vaccination Among Participants Who Were Seropositive at Baseline[6]

End point description:

GMTs were measured using a gpELISA. For participants who were seropositive at baseline (baseline VZV antibody titer ≥1.25 gpELISA units/mL), the percentage of participants with a ≥4-fold rise in VZV antibody titer from Day 1 (baseline) to post-vaccination was assessed and reported for all study arms at 6 weeks post last vaccination (Vaccination 1 for children and Vaccination 2 for adults and adolescents). CIs were only calculated when there were at least 5 participants who were seropositive in a treatment group; missing CIs indicated by "9999". All allocated participants without deviations from the protocol that would substantially affect the results of the immunogenicity outcome measures (Per-Protocol population) who were seropositive at baseline and who received Vaccination 1 (children) or Vaccination 1 and Vaccination 2 (adults and adolescents) were analyzed.

End point type	Primary

End point timeframe:

Day 1 (Baseline), 6 weeks post last vaccination (Day 43 for children and Day 84 for adults and adolescents)

Notes:

[6] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: There were no between-group statistical analyses for this endpoint.

End point values	VARIVAX Adults (18 to 75 years)	VARIVAX™ Adolescents 13 to 17 years of age	VARIVAX™ Children 7 to 12 years of age	VARIVAX™ Children 12 months to 6 years of age
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	23	12	11	3
Units: Percentage of participants				
number (confidence interval 95%)	60.9 (38.5 to 80.3)	66.7 (34.9 to 90.1)	54.5 (23.4 to 83.3)	100.0 (-9999 to 9999)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Solicited Injection-Site Adverse Events (AEs) Post-Vaccination 1

End point title	Percentage of Participants With Solicited Injection-Site Adverse Events (AEs) Post-Vaccination 1

End point description:

An AE was any untoward medical occurrence in a participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. Solicited injection-site AEs, which included erythema, pain, and swelling, were recorded on a Vaccine Report Card (VRC). The percentage of participants who experienced solicited injection-site AEs after Vaccination 1 (up to approximately 5 days post-vaccination) was summarized for all study arms. All allocated participants who received at least one dose of study vaccine and who had some safety follow-up data after the respective vaccination were analyzed.

End point type	Secondary

End point timeframe:

Up to approximately 5 days post-Vaccination 1

End point values	VARIVAX Adults (18 to 75 years)	VARIVAX™ Adolescents 13 to 17 years of age	VARIVAX™ Children 7 to 12 years of age	VARIVAX™ Children 12 months to 6 years of age
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	30	33	37
Units: Percentage of participants				
number (not applicable)				
Injection-site erythema	16.0	3.3	3.0	0.0
Injection-site pain	40.0	23.3	30.3	13.5
Injection-site swelling	10.0	0.0	3.0	0.0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Solicited Injection-Site AEs Post-Vaccination 2

End point title	Percentage of Participants With Solicited Injection-Site AEs Post-Vaccination 2

End point description:

An AE was any untoward medical occurrence in a participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. Solicited injection-site AEs, which included erythema, pain, and swelling, were recorded on a VRC. The percentage of participants who experienced solicited injection-site AEs after Vaccination 2 (up to approximately 5 days post-vaccination) was summarized for all study arms receiving a second vaccination (adults and adolescents). All allocated participants who received two doses of study vaccine (adults and adolescents) and who had some safety follow-up data after the respective vaccination were analyzed. The two children study arms did not receive a second vaccination and were excluded from this analysis

End point type	Secondary

End point timeframe:

Up to approximately 5 days post-Vaccination 2 (up to approximately 46 days)

End point values	VARIVAX Adults (18 to 75 years)	VARIVAX™ Adolescents 13 to 17 years of age	VARIVAX™ Children 7 to 12 years of age	VARIVAX™ Children 12 months to 6 years of age
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	30	0[7]	0[8]
Units: Percentage of participants				
number (not applicable)				
Injection-site erythema	18.4	0		
Injection-site pain	49.0	23.3		
Injection-site swelling	8.2	3.3		

Notes:

[7] - Participants who did not receive a 2nd dose were excluded from analysis.

[8] - Participants who did not receive a 2nd dose were excluded from analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Unsolicited Injection-Site AEs Post-Vaccination 1

End point title	Percentage of Participants With Unsolicited Injection-Site AEs Post-Vaccination 1

End point description:

An AE was any untoward medical occurrence in a participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. Unsolicited injection-site AEs were recorded on a VRC. The percentage of participants who experienced unsolicited injection-site AEs after Vaccination 1 (up to approximately 42 days post-vaccination) was summarized for all study arms. All allocated participants who received at least one dose of study vaccine and who had some safety follow-up data after the respective vaccination were analyzed.

End point type	Secondary

End point timeframe:

Up to approximately 42 days post-Vaccination 1

End point values	VARIVAX Adults (18 to 75 years)	VARIVAX™ Adolescents 13 to 17 years of age	VARIVAX™ Children 7 to 12 years of age	VARIVAX™ Children 12 months to 6 years of age
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	30	33	37
Units: Percentage of participants				
number (not applicable)	2.0	3.3	0.0	5.4

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Unsolicited Injection-Site AEs Post-Vaccination 2

End point title	Percentage of Participants With Unsolicited Injection-Site AEs Post-Vaccination 2

End point description:

An AE was any untoward medical occurrence in a participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. Unsolicited injection-site AEs were recorded on a VRC. The percentage of participants who experienced unsolicited injection-site AEs after Vaccination 2 (up to approximately 42 days post-vaccination) was summarized for all study arms receiving a second vaccination (adults and adolescents). All allocated participants who received two doses of study vaccine (adults and adolescents) and who had some safety follow-up data after the respective vaccination were analyzed. The two children study arms did not receive a second vaccination and were excluded from this analysis.

End point type	Secondary

End point timeframe:

Up to approximately 42 days post-Vaccination 2 (up to approximately 86 days)

End point values	VARIVAX Adults (18 to 75 years)	VARIVAX™ Adolescents 13 to 17 years of age	VARIVAX™ Children 7 to 12 years of age	VARIVAX™ Children 12 months to 6 years of age
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	30	0[9]	0[10]
Units: Percentage of participants				
number (not applicable)	0.0	0.0		

Notes:

[9] - Participants who did not receive a 2nd dose were excluded from analysis.

[10] - Participants who did not receive a 2nd dose were excluded from analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Elevated Temperature Post-Vaccination 1

End point title	Percentage of Participants With Elevated Temperature Post-Vaccination 1

End point description:

The participant's temperature was taken in the evening after Vaccination 1 and daily through Day 28, and was recorded on a VRC. An elevated temperature was defined as ≥39.0 °C (102.2 °F). The percentage of participants with elevated temperature after Vaccination 1 (up to approximately 28 days post-vaccination) was summarized for all study arms. All allocated participants who received at least one dose of study vaccine and who had some safety follow-up data after the respective vaccination were analyzed.

End point type	Secondary

End point timeframe:

Up to 28 days post-Vaccination 1

End point values	VARIVAX Adults (18 to 75 years)	VARIVAX™ Adolescents 13 to 17 years of age	VARIVAX™ Children 7 to 12 years of age	VARIVAX™ Children 12 months to 6 years of age
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	30	33	37
Units: Percentage of participants				
number (not applicable)	2.0	0.0	3.0	8.1

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Elevated Temperature Post-Vaccination 2

End point title	Percentage of Participants With Elevated Temperature Post-Vaccination 2

End point description:

The participant's temperature was taken in the evening after Vaccination 2 and daily through Day 28, and was recorded on a VRC. An elevated temperature was defined as ≥39.0 °C (102.2 °F). The percentage of participants with elevated temperature after Vaccination 2 (up to approximately 28 days post-vaccination) was summarized for all study arms receiving a second vaccination (adults and adolescents). All allocated participants who received two doses of study vaccine (adults and adolescents) and who had some safety follow-up data after the respective vaccination were analyzed. The two children study arms did not receive a second vaccination and were excluded from this analysis.

End point type	Secondary

End point timeframe:

Up to 28 days post-Vaccination 2 (up to approximately 71 days)

End point values	VARIVAX Adults (18 to 75 years)	VARIVAX™ Adolescents 13 to 17 years of age	VARIVAX™ Children 7 to 12 years of age	VARIVAX™ Children 12 months to 6 years of age
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	30	0[11]	0[12]
Units: Percentage of participants				
number (not applicable)	0.0	0.0		

Notes:

[11] - Participants who did not receive a 2nd dose were excluded from analysis.

[12] - Participants who did not receive a 2nd dose were excluded from analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Varicella- and Herpes Zoster-Like Rashes Post-Vaccination 1

End point title	Percentage of Participants With Varicella- and Herpes Zoster-Like Rashes Post-Vaccination 1

End point description:

The development of varicella-like and herpes zoster-like rashes was recorded on a VRC. The percentage of participants who experienced varicella-like and herpes zoster-like rashes after Vaccination 1 (up to approximately 42 days post-vaccination) was summarized for all study arms. All allocated participants who received at least one dose of study vaccine and who had some safety follow-up data after the respective vaccination were analyzed.

End point type	Secondary

End point timeframe:

Up to approximately 42 days post-Vaccination 1

End point values	VARIVAX Adults (18 to 75 years)	VARIVAX™ Adolescents 13 to 17 years of age	VARIVAX™ Children 7 to 12 years of age	VARIVAX™ Children 12 months to 6 years of age
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	30	33	37
Units: Percentage of participants				
number (not applicable)				
Varicella-like rash	6.0	0.0	6.1	2.7
Herpes zoster-like rash	0.0	0.0	0.0	0.0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Varicella- and Herpes Zoster-Like Rashes Post-Vaccination 2

End point title	Percentage of Participants With Varicella- and Herpes Zoster-Like Rashes Post-Vaccination 2

End point description:

The development of varicella-like and herpes zoster-like rashes was recorded on a VRC. The percentage of participants who experienced varicella-like and herpes zoster-like rashes after Vaccination 1 (up to approximately 42 days post-vaccination) was summarized for all study arms receiving a second vaccination (adults and adolescents). All allocated participants who received two doses of study vaccine (adults and adolescents) and who had some safety follow-up data after the respective vaccination were analyzed. The two children study arms did not receive a second vaccination and were excluded from this analysis.

End point type	Secondary

End point timeframe:

Up to approximately 42 days post-Vaccination 2 (up to approximately 86 days)

End point values	VARIVAX Adults (18 to 75 years)	VARIVAX™ Adolescents 13 to 17 years of age	VARIVAX™ Children 7 to 12 years of age	VARIVAX™ Children 12 months to 6 years of age
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	30	0[13]	0[14]
Units: Percentage of participants				
number (not applicable)	2.0	0.0		

Notes:

[13] - Participants who did not receive a 2nd dose were excluded from analysis.

[14] - Participants who did not receive a 2nd dose were excluded from analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Systemic AEs Post-Vaccination 1

End point title	Percentage of Participants With Systemic AEs Post-Vaccination 1

End point description:

An AE was any untoward medical occurrence in a participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. A systemic AE was defined as any non-injection-site AE. Systemic AEs were recorded on a VRC. The percentage of participants who experienced a systemic AE after Vaccination 1 (up to approximately 42 days post-vaccination) was summarized for all study arms. All allocated participants who received at least one dose of study vaccine and who had some safety follow-up data after the respective vaccination were analyzed.

End point type	Secondary

End point timeframe:

Up to approximately 42 days post-Vaccination 1

End point values	VARIVAX Adults (18 to 75 years)	VARIVAX™ Adolescents 13 to 17 years of age	VARIVAX™ Children 7 to 12 years of age	VARIVAX™ Children 12 months to 6 years of age
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	30	33	37
Units: Percentage of participants				
number (not applicable)	38.0	23.3	36.4	43.2

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Systemic AEs Post-Vaccination 2

End point title	Percentage of Participants With Systemic AEs Post-Vaccination 2

End point description:

An AE was any untoward medical occurrence in a participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. A systemic AE was defined as any non-injection-site AE. Systemic AEs were recorded on a VRC. The percentage of participants who experienced a systemic AE after Vaccination 2 (up to approximately 42 days post-vaccination) was summarized for all study arms receiving a second vaccination (adults and adolescents). All allocated participants who received two doses of study vaccine (adults and adolescents) and who had some safety follow-up data after the respective vaccination were analyzed. The two children study arms did not receive a second vaccination and were excluded from this analysis.

End point type	Secondary

End point timeframe:

Up to approximately 42 days post-Vaccination 2 (up to approximately 86 days)

End point values	VARIVAX Adults (18 to 75 years)	VARIVAX™ Adolescents 13 to 17 years of age	VARIVAX™ Children 7 to 12 years of age	VARIVAX™ Children 12 months to 6 years of age
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	30	0[15]	0[16]
Units: Percentage of participants				
number (not applicable)	28.6	26.7		

Notes:

[15] - Participants who did not receive a 2nd dose were excluded from analysis.

[16] - Participants who did not receive a 2nd dose were excluded from analysis.

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With 1 or More Serious Adverse Events (SAEs) Post-Vaccination 1 or Post-Vaccination 2

End point title	Percentage of Participants With 1 or More Serious Adverse Events (SAEs) Post-Vaccination 1 or Post-Vaccination 2

End point description:

An AE was any untoward medical occurrence in a participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. An SAE was an AE that resulted in death, was life-threatening, required inpatient hospitalization or prolongation of existing hospitalization, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect, or another important medical event. The percentage of participants who experienced one or more SAEs after either vaccination (up to approximately 42 days post-vaccination) was summarized for all study arms. All allocated participants who received at least one dose of study vaccine and who had some safety follow-up data after the respective vaccination were analyzed.

End point type	Secondary

End point timeframe:

Up to 42 days post-Vaccination 1 or post-Vaccination 2 (up to approximately 86 days)

End point values	VARIVAX Adults (18 to 75 years)	VARIVAX™ Adolescents 13 to 17 years of age	VARIVAX™ Children 7 to 12 years of age	VARIVAX™ Children 12 months to 6 years of age
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	30	33	37
Units: Percentage of participants				
number (not applicable)	0.0	0.0	3.0	0.0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Vaccine-Related SAEs Post-Vaccination 1 or Post-Vaccination 2

End point title	Percentage of Participants With Vaccine-Related SAEs Post-Vaccination 1 or Post-Vaccination 2

End point description:

An AE was any untoward medical occurrence in a participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. A vaccine-related SAE was an AE that resulted in death, was life-threatening, required inpatient hospitalization or prolongation of existing hospitalization, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect, or another important medical event, that was considered at least possibly related to the study vaccine. The percentage of participants who experienced one or more vaccine-related SAEs

after either vaccination (up to approximately 42 days post-vaccination) was summarized for all study arms. All allocated participants who received at least one dose of study vaccine and who had some safety follow-up data after the respective vaccination were analyzed.

End point type	Secondary

End point timeframe:

Up to 42 days post-Vaccination 1 or post-Vaccination 2 (up to approximately 86 days)

End point values	VARIVAX Adults (18 to 75 years)	VARIVAX™ Adolescents 13 to 17 years of age	VARIVAX™ Children 7 to 12 years of age	VARIVAX™ Children 12 months to 6 years of age
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	30	33	37
Units: Percentage of participants				
number (not applicable)	0.0	0.0	0.0	0.0

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Vaccine-Related Death Post-Vaccination 1 or Post-Vaccination 2

End point title	Percentage of Participants With Vaccine-Related Death Post-Vaccination 1 or Post-Vaccination 2

End point description:

An AE was any untoward medical occurrence in a participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. A vaccine-related SAE was an AE that resulted in death, was life-threatening, required inpatient hospitalization or prolongation of existing hospitalization, resulted in persistent or significant disability/incapacity, was a congenital anomaly/birth defect, or another important medical event, that was considered at least possibly related to the study vaccine. The percentage of participants who experienced a vaccine-related SAE that resulted in death after either vaccination (up to approximately 42 days post-vaccination) was summarized for all study arms. All allocated participants who received at least one dose of study vaccine and who had some safety follow-up data after the respective vaccination were analyzed.

End point type	Secondary

End point timeframe:

Up to 42 days post-Vaccination 1 or post-Vaccination 2 (up to approximately 86 days)

End point values	VARIVAX Adults (18 to 75 years)	VARIVAX™ Adolescents 13 to 17 years of age	VARIVAX™ Children 7 to 12 years of age	VARIVAX™ Children 12 months to 6 years of age
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	30	33	37
Units: Percentage of participants				
number (not applicable)	0.0	0.0	0.0	0.0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 42 days post-Vaccination 1 or post-Vaccination 2 (up to approximately 86 days)

Adverse event reporting additional description:

Serious and Non-serious AE tables include all allocated participants who received at least 1 dose of study vaccination.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.0

Reporting groups

Reporting group title	VARIVAX Adults (18 to 75 years)

Reporting group description:

Participants aged 18 to 75 years of age received 2 doses of VARIVAX™ administered approximately six weeks apart: one 0.5 mL dose of VARIVAX™ administered by subcutaneous (SC) injection on Day 1, and a second 0.5 mL dose of VARIVAX™ by SC injection on Day 43.

Reporting group title	VARIVAX Adolescents (13 to 17 years)

Reporting group description:

Participants aged 13 to 17 years of age received 2 doses of VARIVAX™ administered approximately six weeks apart: one 0.5 mL dose of VARIVAX™ administered by SC injection on Day 1, and a second 0.5 mL dose of VARIVAX™ by SC injection on Day 43.

Reporting group title	VARIVAX Children (7 to 12 years)

Reporting group description:

Participants aged 7 to 12 years of age received one 0.5 mL dose of VARIVAX™ administered by SC injection on Day 1.

Reporting group title	VARIVAX Children (12 months to 6 years)

Reporting group description:

Participants aged 12 months to 6 years of age received one 0.5 mL dose of VARIVAX™ administered by SC injection on Day 1.

Serious adverse events	VARIVAX Adults (18 to 75 years)	VARIVAX Adolescents (13 to 17 years)	VARIVAX Children (7 to 12 years)
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 50 (0.00%)	0 / 30 (0.00%)	1 / 33 (3.03%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 50 (0.00%)	0 / 30 (0.00%)	1 / 33 (3.03%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	VARIVAX Children (12 months to 6		

	years)		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 37 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	VARIVAX Adults (18 to 75 years)	VARIVAX Adolescents (13 to 17 years)	VARIVAX Children (7 to 12 years)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	40 / 50 (80.00%)	17 / 30 (56.67%)	15 / 33 (45.45%)
Investigations			
Body temperature increased			
subjects affected / exposed	6 / 50 (12.00%)	5 / 30 (16.67%)	2 / 33 (6.06%)
occurrences (all)	11	10	2
Nervous system disorders			
Headache			
subjects affected / exposed	9 / 50 (18.00%)	6 / 30 (20.00%)	5 / 33 (15.15%)
occurrences (all)	15	10	5
General disorders and administration site conditions			
Injection site haemorrhage			
subjects affected / exposed	0 / 50 (0.00%)	0 / 30 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Injection site pain			
subjects affected / exposed	29 / 50 (58.00%)	10 / 30 (33.33%)	10 / 33 (30.30%)
occurrences (all)	45	14	10
Injection site erythema			
subjects affected / exposed	16 / 50 (32.00%)	1 / 30 (3.33%)	1 / 33 (3.03%)
occurrences (all)	17	1	1
Injection site swelling			

subjects affected / exposed	7 / 50 (14.00%)	1 / 30 (3.33%)	1 / 33 (3.03%)
occurrences (all)	9	1	1
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 50 (0.00%)	0 / 30 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	3 / 50 (6.00%)	0 / 30 (0.00%)	0 / 33 (0.00%)
occurrences (all)	6	0	0
Skin and subcutaneous tissue disorders			
Rash vesicular			
subjects affected / exposed	3 / 50 (6.00%)	0 / 30 (0.00%)	2 / 33 (6.06%)
occurrences (all)	4	0	2
Infections and infestations			
Respiratory tract infection			
subjects affected / exposed	1 / 50 (2.00%)	0 / 30 (0.00%)	2 / 33 (6.06%)
occurrences (all)	1	0	2
Respiratory tract infection viral			
subjects affected / exposed	1 / 50 (2.00%)	2 / 30 (6.67%)	1 / 33 (3.03%)
occurrences (all)	1	2	1
Rhinitis			
subjects affected / exposed	0 / 50 (0.00%)	0 / 30 (0.00%)	0 / 33 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	VARIVAX Children (12 months to 6 years)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 37 (43.24%)		
Investigations			
Body temperature increased			
subjects affected / exposed	9 / 37 (24.32%)		
occurrences (all)	13		
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
General disorders and administration			

site conditions			
Injection site haemorrhage			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Injection site pain			
subjects affected / exposed	5 / 37 (13.51%)		
occurrences (all)	5		
Injection site erythema			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Injection site swelling			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	0 / 37 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Rash vesicular			
subjects affected / exposed	1 / 37 (2.70%)		
occurrences (all)	1		
Infections and infestations			
Respiratory tract infection			
subjects affected / exposed	5 / 37 (13.51%)		
occurrences (all)	5		
Respiratory tract infection viral			
subjects affected / exposed	4 / 37 (10.81%)		
occurrences (all)	6		
Rhinitis			
subjects affected / exposed	2 / 37 (5.41%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 December 2012	Amendment 1: The primary reason for the amendment was to change the pregnancy/contraceptive follow-up period text so that it was consistent with the Investigator Brochure and the Product Label.
18 April 2013	Amendment 2: The primary reasons for this amendment were to update the study design to include the enrollment targets by age groups and specify the primary immunogenicity and safety endpoints of the study; and to add laboratory tests for participants 7 years of age and older.
03 October 2018	Amendment 3: The primary reasons for this amendment were to edit the title of the study remove "safety" and "tolerability" and to align it with the study's primary focus of immunogenicity, and make its secondary objective that of safety and tolerability. The study design was also revised to include an adult cohort with a target enrollment of 50 participants. This cohort is referred to as Stage 1. Stage 2 would then enroll children and adolescents and follow sequentially after Stage 1. Additionally, the ages of children and adolescent participants in Stage 2 of the study were specified.
18 December 2018	Amendment 4: The primary reason for this amendment was to add an exclusion criterion to exclude participants who had (or their parents had) a documented human immunodeficiency virus (HIV) infection, untreated syphilis infection or viral hepatitis infection (Hepatitis B or C).
30 July 2019	Amendment 5: The primary reason for this amendment was to align the protocol with the current version of the Common Protocol Template (CPT).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported