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	v1
This version publication date	20 December 2020
First version publication date	20 December 2020

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 Russians aged 12 months and older. 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: 100
Worldwide total number of subjects	100
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)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

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

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™ Adolescents 13 to 17 years of age

Arm description:

Participants received one 0.5 mL dose of VARIVAX™ administered by subcutaneous (SC) injection on Day 1. Participants 13 to 17 years of age also received 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:

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

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 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:

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

Number of subjects in period 1	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
Started	30	33	37
Vaccination 1	30	33	37
Vaccination 2	30	0 [1]	0 [2]
Completed	30	33	37

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 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 adolescents 13 to 17 years of age received Vaccination 2.

Baseline characteristics

Reporting groups	
Reporting group title	VARIVAX™ Adolescents 13 to 17 years of age
Reporting group description:	
Participants received one 0.5 mL dose of VARIVAX™ administered by subcutaneous (SC) injection on Day 1. Participants 13 to 17 years of age also received 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 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 received one 0.5 mL dose of VARIVAX™ administered by SC injection on Day 1.	

Reporting group values	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
Number of subjects	30	33	37
Age Categorical Units: Participants			
Age Continuous Units: years			
arithmetic mean	15.1	9.6	3.2
standard deviation	± 1.5	± 1.6	± 1.6
Gender Categorical Units: Participants			
Female	16	14	18
Male	14	19	19
Race Units: Subjects			
White	30	33	37
Serostatus for varicella-zoster virus (VZV)			
A VZV seronegative status at baseline was VZV antibody titer <1.25 glycoprotein enzyme-linked immunosorbent assay (gpELISA) units/mL at baseline. A VZV seropositive status at baseline was a VZV antibody titer ≥1.25 gpELISA units/mL.			
Units: Subjects			
VZV Seronegative	18	22	34
VZV Seropositive	12	11	3

Reporting group values	Total		
Number of subjects	100		
Age Categorical Units: Participants			
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		

Gender Categorical Units: Participants			
Female	48		
Male	52		
Race Units: Subjects			
White	100		
Serostatus for varicella-zoster virus (VZV)			
A VZV seronegative status at baseline was VZV antibody titer <1.25 glycoprotein enzyme-linked immunosorbent assay (gpELISA) units/mL at baseline. A VZV seropositive status at baseline was a VZV antibody titer ≥1.25 gpELISA units/mL.			
Units: Subjects			
VZV Seronegative	74		
VZV Seropositive	26		

End points

End points reporting groups

Reporting group title	VARIVAX™ Adolescents 13 to 17 years of age
Reporting group description:	
Participants received one 0.5 mL dose of VARIVAX™ administered by subcutaneous (SC) injection on Day 1. Participants 13 to 17 years of age also received 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 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 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-Vaccination 2 in Adolescents Who Were Seronegative at Baseline

End point title	Varicella Zoster Virus (VZV) Antibody Response Rate at 6 Weeks Post-Vaccination 2 in Adolescents Who Were Seronegative at Baseline[1][2]
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 VZV antibody titer ≥5 gpELISA units/mL at 6 weeks post-Vaccination 2. The analysis population for this endpoint included all randomized participants without deviations from the protocol who were seronegative at baseline and received Vaccination 1 and Vaccination 2.	
End point type	Primary
End point timeframe:	
6 weeks post-Vaccination 2	

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.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only adolescents 13 to 17 years of age who were seronegative at baseline and received Vaccination 2 were included in this endpoint.

End point values	VARIVAX™ Adolescents 13 to 17 years of age			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: Percentage of participants				
number (confidence interval 95%)	100.0 (81.5 to 100.0)			

Statistical analyses

No statistical analyses for this end point

Primary: VZV Antibody Response Rate at 6 Weeks Post-Vaccination 1 in Children Who Were Seronegative at Baseline

End point title	VZV Antibody Response Rate at 6 Weeks Post-Vaccination 1 in Children Who Were Seronegative at Baseline[3][4]

End point description:

VZV antibody titers were measured using a gpELISA. The VZV antibody response rate was defined as the percentage of participants with VZV antibody titer ≥5 gpELISA units/mL at 6 weeks post-Vaccination 1. The analysis population for this endpoint included all randomized participants without deviations from the protocol who were seronegative at baseline and received Vaccination 1.

End point type	Primary

End point timeframe:

6 weeks post-Vaccination 1

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

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only children 12 months to 6 years of age and 7 to 12 years of age who were seronegative at baseline and received Vaccination 1 were included in this endpoint.

End point values	VARIVAX™ Children 7 to 12 years of age	VARIVAX™ Children 12 months to 6 years of age		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	34		
Units: Percentage of participants				
number (confidence interval 95%)	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-Vaccination 2 in Adolescents Who Were Seronegative at Baseline

End point title	Geometric Mean Titers (GMTs) of VZV Antibodies at 6 Weeks Post-Vaccination 2 in Adolescents Who Were Seronegative at Baseline[5][6]

End point description:

Geometric mean titers of VZV antibodies were measured at 6 weeks post-Vaccination 2 using a gpELISA. The analysis population for this endpoint included all randomized participants without deviations from the protocol who were seronegative at baseline and received Vaccination 1 and Vaccination 2.

End point type	Primary

End point timeframe:

6 weeks post-Vaccination 2

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

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only adolescents 13 to 17 years of age who were seronegative at baseline and received Vaccination 2 were included in this endpoint.

End point values	VARIVAX™ Adolescents 13 to 17 years of age			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: gpELISA units/mL				
geometric mean (confidence interval 95%)	78.6 (46.5 to 133.0)			

Statistical analyses

No statistical analyses for this end point

Primary: GMTs of VZV Antibodies at 6 Weeks Post-Vaccination 1 in Children Who Were Seronegative at Baseline

End point title	GMTs of VZV Antibodies at 6 Weeks Post-Vaccination 1 in Children Who Were Seronegative at Baseline[7][8]

End point description:

Geometric mean titers of VZV antibodies were measured at 6 weeks post-Vaccination 1 using a gpELISA. The analysis population for this endpoint included all randomized participants without deviations from the protocol who were seronegative at baseline and received Vaccination 1.

End point type	Primary

End point timeframe:

6 weeks post-Vaccination 1

Notes:

[7] - 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

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only children 12 months to 6 years of age and 7 to 12 years of age who were seronegative at baseline and received Vaccination 1 were included in this endpoint.

End point values	VARIVAX™ Children 7 to 12 years of age	VARIVAX™ Children 12 months to 6 years of age		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	34		
Units: gpELISA units/mL				
geometric mean (confidence interval 95%)	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-Vaccination 2 in Adolescents Who Were Seronegative at Baseline

End point title	VZV Antibody Seroconversion Rate at 6 Weeks Post-Vaccination 2 in Adolescents Who Were Seronegative at Baseline[9][10]

End point description:

VZV antibody levels were measured using a gpELISA. The seroconversion rate was defined as the percentage of participants with VZV antibodies ≥1.25 gpELISA units/mL at 6 weeks post-Vaccination 2. The analysis population for this endpoint included all randomized participants without deviations from the protocol who were seronegative at baseline and received Vaccination 1 and Vaccination 2.

End point type	Primary

End point timeframe:

6 weeks post-Vaccination 2

Notes:

[9] - 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

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only adolescents 13 to 17 years of age who were seronegative at baseline and received Vaccination 2 were included in this endpoint.

End point values	VARIVAX™ Adolescents 13 to 17 years of age			
Subject group type	Reporting group			
Number of subjects analysed	18			
Units: Percentage of participants				
number (confidence interval 95%)	100.0 (81.5 to 100.0)			

Statistical analyses

No statistical analyses for this end point

Primary: VZV Antibody Seroconversion Rate at 6 Weeks Post-Vaccination 1 in Children Who Were Seronegative at Baseline

End point title	VZV Antibody Seroconversion Rate at 6 Weeks Post-Vaccination 1 in Children Who Were Seronegative at Baseline[11][12]

End point description:

VZV antibody levels were measured using a gpELISA. The seroconversion rate was defined as the percentage of participants with VZV antibodies ≥1.25 gpELISA units/mL at 6 weeks post-Vaccination 1. The analysis population for this endpoint included all randomized participants without deviations from the protocol who were seronegative at baseline and received Vaccination 1.

End point type	Primary

End point timeframe:

6 weeks post-Vaccination 1

Notes:

[11] - 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

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline

period.

Justification: Only children 12 months to 6 years of age and 7 to 12 years of age who were seronegative at baseline and received Vaccination 1 were included in this endpoint.

End point values	VARIVAX™ Children 7 to 12 years of age	VARIVAX™ Children 12 months to 6 years of age		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	22	34		
Units: Percentage of participants				
number (confidence interval 95%)	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-Vaccination 2 in Adolescents Who Were Seropositive at Baseline

End point title	GMTs of VZV Antibodies at Day 1 and 6 Weeks Post-Vaccination 2 in Adolescents Who Were Seropositive at Baseline[13][14]

End point description:

GMTs of VZV antibodies were measured using a gpELISA. The analysis population for this endpoint included all randomized participants without deviations from the protocol who were seropositive at baseline and received Vaccination 1 and Vaccination 2.

End point type	Primary

End point timeframe:

Day 1 and 6 weeks post-Vaccination 2

Notes:

[13] - 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

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only adolescents 13 to 17 years of age who were seropositive at baseline and received Vaccination 2 were included in this endpoint.

End point values	VARIVAX™ Adolescents 13 to 17 years of age			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: gpELISA units/mL				
geometric mean (confidence interval 95%)				
Baseline	13.4 (5.8 to 31.0)			
Post-Vaccination 2	151.7 (92.5 to 248.6)			

Statistical analyses

No statistical analyses for this end point

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

End point title	GMTs of VZV Antibodies at Day 1 and 6 Weeks Post-Vaccination 1 in Children Who Were Seropositive at Baseline[15][16]

End point description:

Geometric mean titers of VZV antibodies were measured using a gpELISA. The analysis population for this endpoint included all randomized participants without deviations from the protocol who were seropositive at baseline and received Vaccination 1. Note: Confidence intervals were only calculated when there were at least 5 participants who were seropositive in a treatment group.

End point type	Primary

End point timeframe:

Day 1 and 6 weeks post-Vaccination 1

Notes:

[15] - 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.

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only children 12 months to 6 years of age and 7 to 12 years of age who were seropositive at baseline and received Vaccination 1 were included in this endpoint.

End point values	VARIVAX™ Children 7 to 12 years of age	VARIVAX™ Children 12 months to 6 years of age		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	3		
Units: gpELISA units/mL				
geometric mean (confidence interval 95%)				
Baseline	24.8 (7.2 to 85.5)	4.2 (-99999.99999 to 99999.99999)		
Post-Vaccination 1	125.0 (37.9 to 411.7)	47.6 (-99999.99999 to 99999.99999)		

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-Vaccination 2 in Adolescents Who Were Seropositive at Baseline

End point title	Geometric Mean Fold Rise (GMFR) in VZV Antibody Titers From Day 1 to 6 Weeks Post-Vaccination 2 in Adolescents Who Were Seropositive at Baseline[17][18]

End point description:

GMTs were measured using a gpELISA. The GMFR was the ratio of the VZV antibody concentration at 6 weeks post-Vaccination 2 to the VZV antibody concentration at Day 1 (baseline). The analysis population for this endpoint included all randomized participants without deviations from the protocol who were seropositive at baseline and received Vaccination 1 and Vaccination 2.

End point type	Primary

End point timeframe:

Day 1 (baseline) and 6 weeks post-Vaccination 2

Notes:

[17] - 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: Only adolescents 13 to 17 years of age who were seropositive at baseline and received Vaccination 2 were included in this endpoint.
[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only adolescents 13 to 17 years of age who were seropositive at baseline and received Vaccination 2 were included in this endpoint.

End point values	VARIVAX™ Adolescents 13 to 17 years of age			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Ratio				
geometric mean (confidence interval 95%)	11.3 (4.6 to 27.5)			

Statistical analyses

No statistical analyses for this end point

Primary: GMFR in VZV Antibody Titers From Day 1 to 6 Weeks Post-Vaccination 1 in Children Who Were Seropositive at Baseline

End point title	GMFR in VZV Antibody Titers From Day 1 to 6 Weeks Post-Vaccination 1 in Children Who Were Seropositive at Baseline[19][20]

End point description:

GMTs were measured using a gpELISA. The GMFR was the ratio of the VZV antibody concentration at 6 weeks post-Vaccination 1 to the VZV antibody concentration at Day 1 (baseline). The analysis population for this endpoint included all randomized participants without deviations from the protocol who were seropositive at baseline and received Vaccination 1. Note: Confidence intervals were only calculated when there were at least 5 participants who were seropositive in a treatment group.

End point type	Primary

End point timeframe:

Day 1 (baseline) and 6 weeks post-Vaccination 1

Notes:

[19] - 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.

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only children 12 months to 6 years of age and 7 to 12 years of age who were seropositive at baseline and received Vaccination 1 were included in this endpoint.

End point values	VARIVAX™ Children 7 to 12 years of age	VARIVAX™ Children 12 months to 6 years of age		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	3		
Units: Ratio				
geometric mean (confidence interval 95%)	5.0 (2.6 to 9.7)	11.2 (-99999.99999 to 99999.99999)		

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-Vaccination 2 in Adolescents 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-Vaccination 2 in Adolescents Who Were Seropositive at Baseline[21][22]

End point description:

The percentage of participants with a ≥4-fold rise from Day 1 baseline (≥1.25gpELISA units/mL) to 6 weeks post-Vaccination 2 was assessed. The analysis population for this endpoint included all randomized participants without deviations from the protocol who were seropositive at baseline and received Vaccination 1 and Vaccination 2.

End point type	Primary

End point timeframe:

Day 1 (baseline) and 6 weeks post-Vaccination 2

Notes:

[21] - 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.

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only adolescents 13 to 17 years of age who were seropositive at baseline and received Vaccination 2 were included in this endpoint.

End point values	VARIVAX™ Adolescents 13 to 17 years of age			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Percentage of participants				
number (confidence interval 95%)	66.7 (34.9 to 90.1)			

Statistical analyses

No statistical analyses for this end point

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

End point title	Percentage of Participants With ≥4-Fold Rise in VZV Antibody Titers From Day 1 to 6 Weeks Post-Vaccination 1 in Children Who Were Seropositive at Baseline[23][24]

End point description:

The percentage of participants with a ≥4-fold rise from Day 1 baseline (≥1.25gpELISA units/mL) to 6 weeks post-Vaccination 1 was assessed. The analysis population for this endpoint included all randomized participants without deviations from the protocol who were seropositive at baseline and received Vaccination 1. Note: Confidence intervals were only calculated when there were at least 5 participants who were seropositive in a treatment group.

End point type	Primary

End point timeframe:

Day 1 (baseline) and 6 weeks post-Vaccination 1

Notes:

[23] - 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.

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only children 12 months to 6 years of age and 7 to 12 years of age who were seropositive at baseline and received Vaccination 1 were included in this endpoint.

End point values	VARIVAX™ Children 7 to 12 years of age	VARIVAX™ Children 12 months to 6 years of age		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	3		
Units: Percentage of participants				
number (confidence interval 95%)	54.5 (23.4 to 83.3)	100.0 (-99999.99999 to 99999.99999)		

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:

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 was summarized. The analysis population for this end point included all randomized participants who received Vaccination 1.

End point type	Secondary

End point timeframe:

Up to 5 days post-Vaccination 1

End point values	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	
Number of subjects analysed	30	33	37	
Units: Percentage of participants				
number (not applicable)				
Injection-site erythema	3.3	3.0	0.0	
Injection-site pain	23.3	30.3	13.5	
Injection-site swelling	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[25]

End point description:

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 was summarized. The analysis population for this end point included all randomized participants who received Vaccination 2.

End point type	Secondary

End point timeframe:

Up to 5 days post-Vaccination 2

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only adolescents 13 to 17 years of age who received Vaccination 2 were included in this endpoint.

End point values	VARIVAX™ Adolescents 13 to 17 years of age			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Percentage of participants				

number (not applicable)				
Injection-site erythema	0.0			
Injection-site pain	23.3			
Injection-site swelling	3.3			

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:

Unsolicited injection-site AEs were recorded on a VRC. The percentage of participants who experienced unsolicited injection-site AEs after Vaccination 1 was summarized. The analysis population for this end point included all randomized participants who received Vaccination 1.

End point type	Secondary

End point timeframe:

Up to 42 days post-Vaccination 1

End point values	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	
Number of subjects analysed	30	33	37	
Units: Percentage of participants				
number (not applicable)	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[26]

End point description:

Unsolicited injection-site AEs were recorded on a VRC. The percentage of participants who experienced unsolicited injection-site AEs after Vaccination 2 was summarized. The analysis population for this end point included all randomized participants who received Vaccination 2.

End point type	Secondary

End point timeframe:

Up to 42 days post-Vaccination 2

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only adolescents 13 to 17 years of age who received Vaccination 2 were included in this endpoint.

End point values	VARIVAX™ Adolescents 13 to 17 years of age			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Percentage of participants				
number (not applicable)	0.0			

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 an elevated temperature was summarized. The analysis population for this end point included all randomized participants who received Vaccination 1.

End point type	Secondary

End point timeframe:

Up to 28 days post-Vaccination 1

End point values	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	
Number of subjects analysed	30	33	37	
Units: Percentage of participants				
number (not applicable)	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[27]

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 an elevated temperature was summarized. The analysis population for this end point included all randomized participants who received Vaccination 2.

End point type	Secondary

End point timeframe:

Up to 28 days post-Vaccination 2

Notes:

[27] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only adolescents 13 to 17 years of age who received Vaccination 2 were included in this endpoint

End point values	VARIVAX™ Adolescents 13 to 17 years of age			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Percentage of participants				
number (not applicable)	0.0			

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 with varicella-like and herpes zoster-like rashes was summarized. The analysis population for this end point included all randomized participants who received Vaccination 1.

End point type	Secondary

End point timeframe:

Up to 42 days post-Vaccination 1

End point values	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	
Number of subjects analysed	30	33	37	
Units: Percentage of participants				
number (not applicable)				
Varicella-like rash	0.0	6.1	2.7	

Herpes zoster-like rash	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[28]

End point description:

The development of varicella-like and herpes zoster-like rashes was recorded on a VRC. The percentage of participants with varicella-like and herpes zoster-like rashes was summarized. The analysis population for this end point included all randomized participants who received Vaccination 2.

End point type	Secondary

End point timeframe:

Up to 42 days post-Vaccination 2

Notes:

[28] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only adolescents 13 to 17 years of age who received Vaccination 2 were included in this endpoint.

End point values	VARIVAX™ Adolescents 13 to 17 years of age			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Percentage of participants				
number (not applicable)	0.0			

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:

A systemic AE was defined as any non-injection-site AE. An AE is defined as any untoward medical occurrence in a participant which does not necessarily have a causal relationship with study drug. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of study drug or a protocol-specified procedure, whether or not considered related to the study drug or protocol-specified procedure. Any worsening of a preexisting condition that is temporally associated with the study drug or protocol-specified procedure is also an AE. Systemic AEs were recorded on a VRC. The percentage of participants who experienced a systemic AE was summarized. The analysis population for this end point included all randomized participants who received Vaccination 1.

End point type	Secondary

End point timeframe:

Up to 42 days post-Vaccination 1

End point values	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	
Number of subjects analysed	30	33	37	
Units: Percentage of participants				
number (not applicable)	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[29]

End point description:

A systemic AE was defined as any non-injection-site AE. An AE is defined as any untoward medical occurrence in a participant which does not necessarily have a causal relationship with study drug. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of study drug or a protocol-specified procedure, whether or not considered related to the study drug or protocol-specified procedure. Any worsening of a preexisting condition that is temporally associated with the study drug or protocol-specified procedure is also an AE. The participant was to record the presence of any VRC-prompted systemic AEs that occurred up to 42 days post-Vaccination 2. The percentage of participants with a systemic AE was summarized. The analysis population for this end point included all randomized participants who received Vaccination 2.

End point type	Secondary

End point timeframe:

Up to 42 days post-Vaccination 2

Notes:

[29] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only adolescents 13 to 17 years of age who received Vaccination 2 were included in this endpoint.

End point values	VARIVAX™ Adolescents 13 to 17 years of age			
Subject group type	Reporting group			
Number of subjects analysed	30			
Units: Percentage of participants				
number (not applicable)	26.7			

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 SAE is an AE that results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, or another important medical event. The percentage of participants with 1 or more SAEs was summarized. The analysis population for this end point included all randomized participants who received at least 1 dose of study vaccination.

End point type	Secondary

End point timeframe:

Up to 42 days post-Vaccination 1 or post-Vaccination 2

End point values	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	
Number of subjects analysed	30	33	37	
Units: Percentage of participants				
number (not applicable)	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:

A vaccine-related SAE is an AE that results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, or another important medical event that is considered at least possibly related to the study vaccine. The percentage of participants that experienced 1 or more vaccine-related SAEs was summarized. The analysis population for this end point included all randomized participants who received at least 1 dose of study vaccination.

End point type	Secondary

End point timeframe:

Up to 42 days post-Vaccination 1 or post-Vaccination 2

End point values	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	
Number of subjects analysed	30	33	37	
Units: Percentage of participants				
number (not applicable)	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:

The percentage of participants that experienced 1 or more SAEs that were considered at least possibly related to the study vaccine and resulted in a death was summarized. The analysis population for this end point included all randomized participants who received at least 1 dose of study vaccination.

End point type	Secondary

End point timeframe:

Up to 42 days post-Vaccination 1 or post-Vaccination 2

End point values	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	
Number of subjects analysed	30	33	37	
Units: Percentage of participants				
number (not applicable)	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

Adverse event reporting additional description:

The safety population included all randomized 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 Children (7 to 12 years)
Reporting group description: -	
Reporting group title	VARIVAX Children (12 months to 6 years)
Reporting group description: -	
Reporting group title	VARIVAX Adolescents (13 to 17 years)
Reporting group description: -	

Serious adverse events	VARIVAX Children (7 to 12 years)	VARIVAX Children (12 months to 6 years)	VARIVAX Adolescents (13 to 17 years)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 33 (3.03%)	0 / 37 (0.00%)	0 / 30 (0.00%)
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	1 / 33 (3.03%)	0 / 37 (0.00%)	0 / 30 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	VARIVAX Children (7 to 12 years)	VARIVAX Children (12 months to 6 years)	VARIVAX Adolescents (13 to 17 years)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 33 (42.42%)	16 / 37 (43.24%)	16 / 30 (53.33%)
Investigations			

Body temperature increased			
subjects affected / exposed	2 / 33 (6.06%)	9 / 37 (24.32%)	5 / 30 (16.67%)
occurrences (all)	2	13	10
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 33 (15.15%)	0 / 37 (0.00%)	6 / 30 (20.00%)
occurrences (all)	5	0	10
General disorders and administration site conditions			
Injection site haemorrhage			
subjects affected / exposed	0 / 33 (0.00%)	2 / 37 (5.41%)	0 / 30 (0.00%)
occurrences (all)	0	2	0
Injection site pain			
subjects affected / exposed	10 / 33 (30.30%)	5 / 37 (13.51%)	10 / 30 (33.33%)
occurrences (all)	10	5	14
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 33 (0.00%)	2 / 37 (5.41%)	0 / 30 (0.00%)
occurrences (all)	0	2	0
Skin and subcutaneous tissue disorders			
Rash vesicular			
subjects affected / exposed	2 / 33 (6.06%)	1 / 37 (2.70%)	0 / 30 (0.00%)
occurrences (all)	2	1	0
Infections and infestations			
Respiratory tract infection			
subjects affected / exposed	2 / 33 (6.06%)	5 / 37 (13.51%)	0 / 30 (0.00%)
occurrences (all)	2	5	0
Respiratory tract infection viral			
subjects affected / exposed	1 / 33 (3.03%)	4 / 37 (10.81%)	2 / 30 (6.67%)
occurrences (all)	1	6	2
Rhinitis			
subjects affected / exposed	0 / 33 (0.00%)	2 / 37 (5.41%)	0 / 30 (0.00%)
occurrences (all)	0	2	0

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