Clinical trial results:
A Phase 3, Double-Blind, Randomized, Multicenter, Controlled Study to Evaluate the Immunogenicity, Safety, and Tolerability of VARIVAX™ Passage Extension 34 (PE34) Process Administered Concomitantly with M-M-R™ II

Summary

EudraCT number	2017-001910-27
Trial protocol	Outside EU/EEA
Global end of trial date	02 April 2019

Results information

Result version number	v1 (current)
This version publication date	21 September 2019
First version publication date	21 September 2019

Trial information

Trial identification

Sponsor protocol code	V210-A03

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03239873
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	02 April 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 August 2018
Global end of trial reached?	Yes
Global end of trial date	02 April 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study evaluated the immunogenicity, safety, and tolerability of VARIVAX® (Varicella Virus Vaccine Live) manufactured with a new passage extension (PE34) process compared with the VARIVAX® 2016 commercial process. The primary hypotheses being tested were that antibody response rate and mean antibody titer induced at 6 weeks after a single vaccination by VARIVAX® PE34 Process are non-inferior to those induced by VARIVAX® 2016 commercial process, and that antibody response rate induced by VARIVAX® PE34 Process is acceptable.

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	17 October 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 600
Worldwide total number of subjects	600
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)	600
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Eligible participants were randomly assigned in a 1:1 ratio to receive 2 doses of either VARIVAX® Passage Extension 34 (PE34) process or VARIVAX® (2016 commercial product [CP]), given concomitantly with measles, mumps, and rubella (M-M-R)® II approximately 3 months apart.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	VARIVAX PE34 + M-M-R II

Arm description:

VARIVAX® Passage Extension 34 (PE34) Process 0.5 mL administered in the left arm and M-M-R®II vaccine 0.5 mL administered in the right arm by subcutaneous injection on Day 1 and Day 91.

Arm type	Experimental
Investigational medicinal product name	M-M-R®II vaccine
Investigational medicinal product code	
Other name	Measles, Mumps, and Rubella Virus Vaccine Live
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Single 0.5 mL dose suspension for subcutaneous injection after reconstitution

Investigational medicinal product name	VARIVAX® Passage Extension 34 (PE34) process
Investigational medicinal product code	
Other name	Varicella Virus Vaccine Live PE34 process
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Single 0.5 mL dose suspension for subcutaneous injection after reconstitution

Arm title	VARIVAX (2016 CP) + M-M-R II

Arm description:

2016 Commercial Process vaccine 0.5 mL administered in the left arm or thigh and M-M-R® II vaccine 0.5 mL administered in the right arm or thigh by subcutaneous injection on Day 1 and Day 91.

Arm type	Active comparator
Investigational medicinal product name	M-M-R® II vaccine
Investigational medicinal product code	
Other name	Measles, Mumps, and Rubella Virus Vaccine Live
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Single 0.5 mL dose suspension for subcutaneous injection after

reconstitution

Investigational medicinal product name	VARIVAX® 2016 Commercial Process vaccine
Investigational medicinal product code	
Other name	Varicella Virus Vaccine Live (2016 commercial product)
Pharmaceutical forms	Injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Single 0.5 mL dose suspension for subcutaneous injection after reconstitution

Number of subjects in period 1	VARIVAX PE34 + M-M-R II	VARIVAX (2016 CP) + M-M-R II
Started	300	300
Vaccination 1	299	300
Vaccination 2	276	282
Completed	268	273
Not completed	32	27
Physician decision	1	-
Consent withdrawn by subject	2	-
Contraindication to study medication	1	-
Withdrawal by Parent/Guardian	12	11
Lost to follow-up	15	16
Protocol deviation	1	-

Baseline characteristics

Reporting groups	
Reporting group title	VARIVAX PE34 + M-M-R II
Reporting group description:	
VARIVAX® Passage Extension 34 (PE34) Process 0.5 mL administered in the left arm and M-M-R®II vaccine 0.5 mL administered in the right arm by subcutaneous injection on Day 1 and Day 91.	
Reporting group title	VARIVAX (2016 CP) + M-M-R II
Reporting group description:	
2016 Commercial Process vaccine 0.5 mL administered in the left arm or thigh and M-M-R® II vaccine 0.5 mL administered in the right arm or thigh by subcutaneous injection on Day 1 and Day 91.	

Reporting group values	VARIVAX PE34 + M-M-R II	VARIVAX (2016 CP) + M-M-R II	Total
Number of subjects	300	300	600
Age categorical			
Units: Subjects			
Age Continuous			
Units: months			
arithmetic mean	13.0	13.2	
standard deviation	± 1.4	± 1.7	-
Sex: Female, Male			
Units: Subjects			
Female	153	127	280
Male	147	173	320
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	1	0	1
Asian	4	6	10
Native Hawaiian or Other Pacific Islander	0	1	1
Black or African American	35	23	58
White	237	239	476
More than one race	23	31	54
Unknown or Not Reported	0	0	0
Ethnicity			
Units: Subjects			
Hispanic or Latino	46	60	106
Not Hispanic or Latino	254	237	491
Unknown or Not Reported	0	3	3

End points

End points reporting groups	
Reporting group title	VARIVAX PE34 + M-M-R II
Reporting group description:	
VARIVAX® Passage Extension 34 (PE34) Process 0.5 mL administered in the left arm and M-M-R®II vaccine 0.5 mL administered in the right arm by subcutaneous injection on Day 1 and Day 91.	
Reporting group title	VARIVAX (2016 CP) + M-M-R II
Reporting group description:	
2016 Commercial Process vaccine 0.5 mL administered in the left arm or thigh and M-M-R® II vaccine 0.5 mL administered in the right arm or thigh by subcutaneous injection on Day 1 and Day 91.	

Primary: Percentage of Participants with Varicella Zoster Virus Antibody Levels ≥5 Glycoprotein Enzyme-linked Immunosorbent Assay Units/mL

End point title	Percentage of Participants with Varicella Zoster Virus Antibody Levels ≥5 Glycoprotein Enzyme-linked Immunosorbent Assay Units/mL
End point description:	
The varicella zoster virus (VZV) antibody response rate was defined as the percentage of participants with VZV antibody titer ≥5 glycoprotein enzyme-linked immunosorbent assay (gpELISA) units/mL among participants who were seronegative to VZV (titers <1.25 gpELISA units/mL) at baseline. The analysis population included the number of participants with seronegative antibody titer (<1.25 gpELISA units/mL) at baseline and postvaccination serology.	
End point type	Primary
End point timeframe:	
6 weeks (43 days) after vaccination 1	

End point values	VARIVAX PE34 + M-M-R II	VARIVAX (2016 CP) + M-M-R II		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	245	239		
Units: Percentage of Participants				
number (confidence interval 95%)	98.4 (95.9 to 99.6)	98.3 (95.8 to 99.5)		

Statistical analyses

Statistical analysis title	Non-Inferiority
Comparison groups	VARIVAX PE34 + M-M-R II v VARIVAX (2016 CP) + M-M-R II
Number of subjects included in analysis	484
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Risk difference (RD)
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.7
upper limit	2.8

Notes:

[1] - The statistical criterion for non-inferiority of the response rate corresponds to the lower bound of the 2-sided 95% confidence interval [CI] on the difference in response rates [VARIVAX® PE34 process minus VARIVAX® 2016 commercial product] excluding a decrease of 10 percentage points or more.

Statistical analysis title	VARIVAX PE34 Acceptability

Statistical analysis description:

The conclusion of acceptability is based on the lower bound of the 95% Confidence Interval (CI) being >76%, and implies that the value of the parameter is statistically significantly greater than the prespecified acceptability criterion (76%).

Comparison groups	VARIVAX PE34 + M-M-R II v VARIVAX (2016 CP) + M-M-R II
Number of subjects included in analysis	484
Analysis specification	Pre-specified
Analysis type	other[2]
P-value	< 0.001
Method	Exact CI method/binomial proportion
Parameter estimate	Antibody Response Rate
Point estimate	98.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	95.9
upper limit	99.6

Notes:

[2] - Acceptability

Primary: Geometric Mean Titer of VZV Antibodies

End point title	Geometric Mean Titer of VZV Antibodies

End point description:

The geometric mean titer (GMT) of VZV antibodies was measured with gpELISA. The analysis population included the number of participants with seronegative antibody titer (< 1.25 gpELISA units/mL) at baseline and postvaccination serology.

End point type	Primary

End point timeframe:

6 weeks (43 days) after vaccination 1

End point values	VARIVAX PE34 + M-M-R II	VARIVAX (2016 CP) + M-M-R II		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	245	239		
Units: gpELISA units/mL				
geometric mean (confidence interval 95%)	18.5 (17.1 to 20.1)	19.0 (17.6 to 20.5)		

Statistical analyses

Statistical analysis title	Non-Inferiority
Comparison groups	VARIVAX PE34 + M-M-R II v VARIVAX (2016 CP) + M-M-R II
Number of subjects included in analysis	484
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
P-value	< 0.001
Method	Miettinen and Nurminen
Parameter estimate	Risk difference (RD)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.9
upper limit	1.1

Notes:

[3] - The statistical criterion for noninferiority of the GMT corresponds to the lower bound of the 2-sided 95% CI on the GMT ratio [VARIVAX® PE34 process/VARIVAX® 2016 commercial product] being >0.67.

Secondary: Percentage of Participants with Fever (≥102.2 °F Oral Equivalent)

End point title	Percentage of Participants with Fever (≥102.2 °F Oral Equivalent)

End point description:

The percentage of participants with fever ≥102.2 °F oral equivalent for Day 1 through Day 42 after vaccination 1 and Day 1 through Day 42 after vaccination 2 was reported. The analysis population consisted of all randomized/allocated participants who received at least 1 vaccination of study treatment with temperature data at the time of assessment.

End point type	Secondary

End point timeframe:

Up to 42 days after vaccination 1; Up to 42 days after vaccination 2

End point values	VARIVAX PE34 + M-M-R II	VARIVAX (2016 CP) + M-M-R II		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	299	300		
Units: Percentage of Participants				
number (not applicable)				
Up to 42 days after Vaccination 1 (n=299, n=300)	11.8	9.8		
Up to 42 days after Vaccination 2 (n=276, n=282)	8.9	6.1		

Statistical analyses

Statistical analysis title	Vac 1 Fever: VARIVAX PE34 vs VARIVAX (2016 CP)
Comparison groups	VARIVAX PE34 + M-M-R II v VARIVAX (2016 CP) + M-M-R II
Number of subjects included in analysis	599
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.436
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.1
upper limit	7.1

Statistical analysis title	Vac 2 Fever: VARIVAX PE34 vs VARIVAX (2016 CP)
Comparison groups	VARIVAX PE34 + M-M-R II v VARIVAX (2016 CP) + M-M-R II
Number of subjects included in analysis	599
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.204
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.6
upper limit	7.5

Secondary: Percentage of Participants with Systemic Measles-Like, Rubella-Like, Varicella-Like, Zoster-Like Rash, and Mumps-Like Symptoms after Vaccination 1 (Incidence > 0%)

End point title	Percentage of Participants with Systemic Measles-Like, Rubella-Like, Varicella-Like, Zoster-Like Rash, and Mumps-Like Symptoms after Vaccination 1 (Incidence > 0%)

End point description:

The percentage of participants with measles-like, rubella-like, varicella-like, zoster-like rash, and mumps-like symptoms after vaccination 1 was assessed. A specific adverse event was reported only if

its incidence was >0% in one or more vaccination groups after rounding. The analysis population consisted of all randomized/allocated participants who received at least 1 vaccination of study treatment with data at the time of assessment.

End point type	Secondary

End point timeframe:

Up to 42 days after vaccination 1

End point values	VARIVAX PE34 + M-M-R II	VARIVAX (2016 CP) + M-M-R II		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	299	300		
Units: Percentage of Participants				
number (not applicable)				
Measles-like rash	0.3	1.7		
Rubella-like rash	0.3	0.0		
Varicella-like rash	2.7	1.3		
Zoster-like rash	0.0	0.3		

Statistical analyses

Statistical analysis title	Vac 1: Measles-like rash
Comparison groups	VARIVAX PE34 + M-M-R II v VARIVAX (2016 CP) + M-M-R II
Number of subjects included in analysis	599
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.102
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	-1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.5
upper limit	0.4

Statistical analysis title	Vac 1: Rubella-like rash
Comparison groups	VARIVAX PE34 + M-M-R II v VARIVAX (2016 CP) + M-M-R II
Number of subjects included in analysis	599
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.317
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	0.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.9
upper limit	1.9

Statistical analysis title	Vac 1: Varicella-like rash
Comparison groups	VARIVAX PE34 + M-M-R II v VARIVAX (2016 CP) + M-M-R II
Number of subjects included in analysis	599
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.241
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	1.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	4

Statistical analysis title	Vac 1: Zoster-like rash
Comparison groups	VARIVAX PE34 + M-M-R II v VARIVAX (2016 CP) + M-M-R II
Number of subjects included in analysis	599
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.318
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.9
upper limit	0.9

Secondary: Percentage of Participants with Systemic Measles-Like, Rubella-Like, Varicella-Like, Zoster-Like Rash, and Mumps-Like Symptoms after Vaccination 2 (Incidence > 0%)

End point title	Percentage of Participants with Systemic Measles-Like, Rubella-Like, Varicella-Like, Zoster-Like Rash, and Mumps-Like Symptoms after Vaccination 2 (Incidence > 0%)

End point description:

The percentage of participants with measles-like, rubella-like, varicella-like, zoster-like rash, and mumps-like symptoms after vaccination 2 was assessed. A specific adverse event was reported only if

its incidence was >0% in one or more vaccination groups after rounding. The analysis population consisted of all randomized/allocated participants who received at least 1 vaccination of study treatment with data at the time of assessment.

End point type	Secondary
End point timeframe:	
Up to 42 days after vaccination 2	

End point values	VARIVAX PE34 + M-M-R II	VARIVAX (2016 CP) + M-M-R II		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	276	282		
Units: Percentage of Participants				
number (not applicable)				
Measles-like rash	1.4	0.4		
Varicella-like rash	0.4	0.7		
Zoster-like rash	0.4	0.0		

Statistical analyses

Statistical analysis title	Vac 2: Measles-like rash
Comparison groups	VARIVAX PE34 + M-M-R II v VARIVAX (2016 CP) + M-M-R II
Number of subjects included in analysis	558
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.17
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	1.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.7
upper limit	3.4

Statistical analysis title	Vac 2: Varicella-like rash
Comparison groups	VARIVAX PE34 + M-M-R II v VARIVAX (2016 CP) + M-M-R II
Number of subjects included in analysis	558
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.576
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	-0.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.2
upper limit	1.4

Statistical analysis title	Vac 2: Zoster-like rash
Comparison groups	VARIVAX PE34 + M-M-R II v VARIVAX (2016 CP) + M-M-R II
Number of subjects included in analysis	558
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.312
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	2

Secondary: Percentage of Participants with Solicited Injection-Site Erythema, Injection-Site Swelling, and Injection-Site Pain/Tenderness after Vaccination 1

End point title	Percentage of Participants with Solicited Injection-Site Erythema, Injection-Site Swelling, and Injection-Site Pain/Tenderness after Vaccination 1

End point description:

The percentage of participants with solicited (Vaccine Report Card) injection-site erythema, injection-site swelling, and injection-site pain/tenderness was assessed. The analysis population consisted of all randomized/allocated participants who received at least 1 vaccination of study treatment with data at the time of assessment.

End point type	Secondary

End point timeframe:

Up to 5 days after vaccination 1

End point values	VARIVAX PE34 + M-M-R II	VARIVAX (2016 CP) + M-M-R II		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	299	300		
Units: Percentage of Participants				
number (not applicable)				
Injection site erythema	9.7	10.7		
Injection site pain	13.4	12.7		
Injection site swelling	3.0	5.7		

Statistical analyses

Statistical analysis title	Vac 1: Injection-site erythema
Comparison groups	VARIVAX PE34 + M-M-R II v VARIVAX (2016 CP) + M-M-R II
Number of subjects included in analysis	599
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.696
Method	Miettinen & Nurminen
Parameter estimate	Difference of Percentage
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.9
upper limit	4

Statistical analysis title	Vac 1: Injection-site pain
Comparison groups	VARIVAX PE34 + M-M-R II v VARIVAX (2016 CP) + M-M-R II
Number of subjects included in analysis	599
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.796
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.7
upper limit	6.2

Statistical analysis title	Vac 1: Injection-site swelling
Comparison groups	VARIVAX PE34 + M-M-R II v VARIVAX (2016 CP) + M-M-R II

Number of subjects included in analysis	599
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.111
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	-2.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.2
upper limit	0.7

Secondary: Percentage of Participants with Solicited Injection-Site Erythema, Injection-Site Swelling, and Injection-Site Pain/Tenderness after Vaccination 2

End point title	Percentage of Participants with Solicited Injection-Site Erythema, Injection-Site Swelling, and Injection-Site Pain/Tenderness after Vaccination 2

End point description:

The percentage of participants with solicited (Vaccine Report Card) injection-site erythema, injection-site swelling, and injection-site pain/tenderness was assessed. The analysis population consisted of all randomized/allocated participants who received at least 1 vaccination of study treatment with data at the time of assessment.

End point type	Secondary

End point timeframe:

Up to 5 days after vaccination 2

End point values	VARIVAX PE34 + M-M-R II	VARIVAX (2016 CP) + M-M-R II		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	276	282		
Units: Percentage of Participants				
number (not applicable)				
Injection-site erythema	19.6	19.9		
Injection-site pain	8.7	10.3		
Injection-site swelling	10.1	8.2		

Statistical analyses

Statistical analysis title	Vac 2: Injection-site erythema
Comparison groups	VARIVAX PE34 + M-M-R II v VARIVAX (2016 CP) + M-M-R II

Number of subjects included in analysis	558
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.931
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.9
upper limit	6.4

Statistical analysis title	Vac 2: Injection-site swelling
Comparison groups	VARIVAX PE34 + M-M-R II v VARIVAX (2016 CP) + M-M-R II
Number of subjects included in analysis	558
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.415
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.9
upper limit	6.9

Statistical analysis title	Vac 2: Injection-site pain
Comparison groups	VARIVAX PE34 + M-M-R II v VARIVAX (2016 CP) + M-M-R II
Number of subjects included in analysis	558
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.523
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.6
upper limit	3.4

Secondary: Percentage of Participants with One or More Adverse Events

End point title	Percentage of Participants with One or More Adverse Events

End point description:

An adverse event (AE) is any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal product or protocol-specified procedure, whether or not considered related to the medicinal product or protocol-specified procedure. Any worsening (i.e., any clinically significant adverse change in frequency and/or intensity) of a preexisting condition that is temporally associated with the use of the Sponsor's product, is also an AE. The percentage of participants with one or more adverse events for Day 1 through Day 42 after vaccination 1 and Day 1 through Day 42 after vaccination 2 was reported.

End point type	Secondary

End point timeframe:

Up to 42 days after vaccination 1 and up to 42 days after vaccination 2

End point values	VARIVAX PE34 + M-M-R II	VARIVAX (2016 CP) + M-M-R II		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	299	300		
Units: Percentage of Participants				
number (not applicable)	90.0	88.3		

Statistical analyses

Statistical analysis title	Vac 1 & 2: AEs: VARIVAX PE34 vs VARIVAX (2016 CP)
Comparison groups	VARIVAX PE34 + M-M-R II v VARIVAX (2016 CP) + M-M-R II
Number of subjects included in analysis	599
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	6.7

Secondary: Percentage of Participants with One or More Serious Adverse Events

End point title	Percentage of Participants with One or More Serious Adverse Events

End point description:

A serious adverse event (SAE) is defined as an adverse event that resulted in death, was life threatening, resulted in persistent or significant disability or incapacity, resulted in or prolonged a hospitalization, is a congenital anomaly or birth defect, is a cancer, was an overdose, or was an important medical event based on appropriate medical judgment. The percentage of participants with one or more SAEs ~180 days after vaccination 2 was reported. The analysis population consisted of all randomized/allocated participants who received at least 1 vaccination of study treatment with data at

the time of assessment.

End point type	Secondary

End point timeframe:

Up to ~180 days after vaccination 2 (Up to ~285 days)

End point values	VARIVAX PE34 + M-M-R II	VARIVAX (2016 CP) + M-M-R II		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	299	300		
Units: Percentage of Participants				
number (not applicable)	2.0	2.0		

Statistical analyses

Statistical analysis title	All SAEs: VARIVAX PE34 vs VARIVAX (2016 CP)
Comparison groups	VARIVAX PE34 + M-M-R II v VARIVAX (2016 CP) + M-M-R II
Number of subjects included in analysis	599
Analysis specification	Pre-specified
Analysis type	
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.5
upper limit	2.6

Secondary: Percentage of Participants with One or More Vaccine-Related Adverse Events

End point title	Percentage of Participants with One or More Vaccine-Related Adverse Events

End point description:

The percentage of participants with one or more vaccine-related adverse events for Day 1 through Day 42 after vaccination 1 and Day 1 through Day 42 after vaccination 2 was reported. The analysis population consisted of all randomized/allocated participants who received at least 1 vaccination of study treatment with data at the time of assessment.

End point type	Secondary

End point timeframe:

Up to 42 days after vaccination 1 and up to 42 days after vaccination 2

End point values	VARIVAX PE34 + M-M-R II	VARIVAX (2016 CP) + M-M-R II		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	299	300		
Units: Percentage of Participants				
number (not applicable)	56.2	54.3		

Statistical analyses

Statistical analysis title	Vac AEs: VARIVAX PE34 vs VARIVAX (2016 CP)
Comparison groups	VARIVAX PE34 + M-M-R II v VARIVAX (2016 CP) + M-M-R II
Number of subjects included in analysis	599
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.1
upper limit	9.8

Secondary: Percentage of Participants with One or More Systemic Adverse Events after Vaccination 1 (Incidence ≥ 4)

End point title	Percentage of Participants with One or More Systemic Adverse Events after Vaccination 1 (Incidence ≥ 4)

End point description:

All systemic adverse events were recorded on an electronic vaccination report card (eVRC) for Day 1 through Day 42 after vaccination 1. The percentage of participants with one or more systemic adverse events (incidence ≥4 participants in one or more of the vaccination groups) was reported. The analysis population consisted of all randomized/allocated participants who received at least 1 vaccination of study treatment with data at the time of assessment.

End point type	Secondary

End point timeframe:

Up to 42 days after vaccination 1

End point values	VARIVAX PE34 + M-M-R II	VARIVAX (2016 CP) + M-M-R II		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	299	300		
Units: Percentage of Participants				
number (not applicable)	76.6	74.3		

Statistical analyses

Statistical analysis title	Vac 1: Syst AEs: VARIVAX PE34 vs VARIVAX (2016 CP)
Comparison groups	VARIVAX PE34 + M-M-R II v VARIVAX (2016 CP) + M-M-R II
Number of subjects included in analysis	599
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	2.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.7
upper limit	9.2

Secondary: Percentage of Participants with One or More Systemic Adverse Events after Vaccination 2 (Incidence ≥ 0)

End point title	Percentage of Participants with One or More Systemic Adverse Events after Vaccination 2 (Incidence ≥ 0)

End point description:

All systemic adverse events were recorded on an electronic vaccination report card (eVRC) for Day 1 through Day 42 after vaccination 2. The percentage of participants with one or more systemic adverse events was assessed. A specific adverse event was reported only if its incidence was >0% in one or more vaccination groups after rounding. The analysis population consisted of all randomized/allocated participants who received at least 1 vaccination of study treatment with data at the time of assessment.

End point type	Secondary

End point timeframe:

Up to 42 days after vaccination 2

End point values	VARIVAX PE34 + M-M-R II	VARIVAX (2016 CP) + M-M-R II		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	276	282		
Units: Percentage of Participants				
number (not applicable)	60.9	59.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Immunogenicity to Varicella Zoster Virus in Participants Initially Seropositive to Varicella Zoster Virus Antibody (≥ 5gpELISA units/mL)

End point title	Percentage of Participants with Immunogenicity to Varicella Zoster Virus in Participants Initially Seropositive to Varicella Zoster Virus Antibody (≥ 5gpELISA units/mL)

End point description:

The percentage of participants with seropositive antibody titer (≥1.25gpELISA units/mL) at baseline and postvaccination serology contributing to the per-protocol analysis was assessed. Confidence interval is calculated if there are at least 5 subjects who are seropositive. Antibody titers were assessed using gpELISA. The analysis population consisted of all participants with seropositive antibody titer (≥1.25gpELISA units/mL) at baseline and with available postvaccination serology data.

End point type	Secondary

End point timeframe:

6 weeks (43 days) after vaccination 1

End point values	VARIVAX PE34 + M-M-R II	VARIVAX (2016 CP) + M-M-R II		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	40		
Units: Percentage of Participants				
number (confidence interval 95%)	100.0 (88.8 to 100.0)	97.5 (86.8 to 99.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Fold Rise from Baseline in Varicella Zoster Virus Antibody Titers in Participants Initially Seropositive to Varicella Zoster Virus Antibody

End point title	Geometric Mean Fold Rise from Baseline in Varicella Zoster Virus Antibody Titers in Participants Initially Seropositive to Varicella Zoster Virus Antibody

End point description:

Blood samples were taken at pre-vaccination (baseline) and approximately 43 days after vaccination 1 to determine the geometric mean titer (GMT) of VZV antibodies via gpELISA. The geometric mean fold rise (GMFR) was calculated as GMT post vaccination 1/GMT pre-vaccination (baseline). Confidence interval is calculated if there are at least 5 subjects who are seropositive. The analysis population consisted of all participants with with seropositive antibody titers (≥1.25gpELISA units/mL) at baseline and with available postvaccination serology data.

End point type	Secondary

End point timeframe:

Baseline and 6 weeks (~43 days) after vaccination 1

End point values	VARIVAX PE34 + M-M-R II	VARIVAX (2016 CP) + M-M-R II		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	40		
Units: Ratio				
geometric mean (confidence interval 95%)	6.5 (5.0 to 8.5)	7.2 (5.9 to 8.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with a ≥4-Fold Rise From Baseline in Varicella Zoster Virus Antibody Titers in Participants Initially Seropositive to Varicella Zoster Virus

End point title	Percentage of Participants with a ≥4-Fold Rise From Baseline in Varicella Zoster Virus Antibody Titers in Participants Initially Seropositive to Varicella Zoster Virus

End point description:

The percentage of participants with a geometric mean ≥4-fold rise from baseline of ≥1.25gpELISA units/mL in VZV antibody titers at approximately 43 days after vaccination 1 was assessed. The analysis population consisted of all participants with seropositive antibody titers (≥1.25gpELISA units/mL) and available postvaccination serology data.

End point type	Secondary

End point timeframe:

Baseline and 6 weeks (43 days) after vaccination 1

End point values	VARIVAX PE34 + M-M-R II	VARIVAX (2016 CP) + M-M-R II		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	40		
Units: Percentage of Participants				
geometric mean (confidence interval 95%)	80.6 (62.5 to 92.5)	82.5 (67.2 to 92.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with One or More Vaccine-Related Serious Adverse Events

End point title	Percentage of Participants with One or More Vaccine-Related Serious Adverse Events

End point description:

The percentage of participants with one or more vaccine-related serious adverse events up to ~180 days after vaccination 2 was reported. The study investigator determines whether the serious adverse event is related to the vaccine. The analysis population consisted of all randomized/allocated participants who received at least 1 vaccination of study treatment with data at the time of assessment.

End point type	Secondary

End point timeframe:

Up to ~180 days after vaccination 2

End point values	VARIVAX PE34 + M-M-R II	VARIVAX (2016 CP) + M-M-R II		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	299	300		
Units: Percentage of Participants				
number (not applicable)	0.0	0.0		

Statistical analyses

Statistical analysis title	All Vac SAEs: VARIVAX PE34 vs VARIVAX (2016 CP)
Comparison groups	VARIVAX PE34 + M-M-R II v VARIVAX (2016 CP) + M-M-R II
Number of subjects included in analysis	599
Analysis specification	Pre-specified
Analysis type	
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	1.3

Secondary: Percentage of Participants who Discontinued from the Study due to an Adverse Event

End point title	Percentage of Participants who Discontinued from the Study due to an Adverse Event

End point description:

The percentage of participants discontinued from the study due to an adverse event for Day 1 through Day 42 after vaccination 1 and Day 1 through Day 42 after vaccination 2 was reported. The analysis population consisted of all randomized/allocated participants who received at least 1 vaccination of study treatment with data at the time of assessment.

End point type	Secondary

End point timeframe:

Up to 42 days after vaccination 1 and up to 42 days after vaccination 2

End point values	VARIVAX PE34 + M-M-R II	VARIVAX (2016 CP) + M-M-R II		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	299	300		
Units: Percentage of Participants				
number (not applicable)	0.0	0.0		

Statistical analyses

Statistical analysis title	Discontinued: VARIVAX PE34 vs VARIVAX (2016 CP)
Comparison groups	VARIVAX PE34 + M-M-R II v VARIVAX (2016 CP) + M-M-R II
Number of subjects included in analysis	599
Analysis specification	Pre-specified
Analysis type	
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.3
upper limit	1.3

Secondary: Percentage of Participants with One or More Unsolicited Injection-Site Adverse Events after Vaccination 1 (Incidence > 0%)

End point title	Percentage of Participants with One or More Unsolicited Injection-Site Adverse Events after Vaccination 1 (Incidence > 0%)

End point description:

The percentage of participants with unsolicited injection-site adverse events (or AEs not superficially listed on eVRC) for Day 1 through Day 42 after vaccination 1 was assessed. A specific adverse event was reported only if its incidence was >0% in one or more vaccination groups after rounding. The analysis population consisted of all randomized/allocated participants who received at least 1 vaccination of study treatment with data at the time of assessment.

End point type	Secondary

End point timeframe:

Up to 42 days after vaccination 1

End point values	VARIVAX PE34 + M-M-R II	VARIVAX (2016 CP) + M-M-R II		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	299	300		
Units: Percentage of Participants				
number (not applicable)	8.0	9.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with One or More Unsolicited Injection-Site Adverse Events after Vaccination 2 (Incidence > 0%)

End point title	Percentage of Participants with One or More Unsolicited Injection-Site Adverse Events after Vaccination 2 (Incidence > 0%)

End point description:

The percentage of participants with unsolicited injection-site adverse events (or AEs not superficially listed on eVRC) for Day 1 through Day 42 after vaccination 2 was assessed. A specific adverse event was reported only if its incidence was >0% in one or more vaccination groups after rounding. The analysis population consisted of all randomized/allocated participants who received at least 1 vaccination of study treatment with data at the time of assessment.

End point type	Secondary

End point timeframe:

Up to 42 days after vaccination 2

End point values	VARIVAX PE34 + M-M-R II	VARIVAX (2016 CP) + M-M-R II		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	276	282		
Units: Percentage of Participants				
number (not applicable)	1.4	2.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with Medically-Attended Adverse Events (Incidence ≥5%)

End point title	Percentage of Participants with Medically-Attended Adverse Events (Incidence ≥5%)

End point description:

The percentage of participants with medically-attended AEs up to ~180 days after vaccination 2 that did not meet the definition of serious adverse event (incidence ≥5% in one or more vaccination groups) was reported. The analysis population consisted of all randomized/allocated participants who received at least 1 vaccination of study treatment with data at the time of assessment.

End point type	Secondary

End point timeframe:

Up to ~180 days after vaccination 2 (Up to ~285 days)

End point values	VARIVAX PE34 + M-M-R II	VARIVAX (2016 CP) + M-M-R II		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	275	282		
Units: Percentage of Participants				
number (not applicable)	29.5	26.6		

Statistical analyses

Statistical analysis title	Med Att AEs: VARIVAX PE34 vs VARIVAX (2016 CP)
Comparison groups	VARIVAX PE34 + M-M-R II v VARIVAX (2016 CP) + M-M-R II
Number of subjects included in analysis	557
Analysis specification	Pre-specified
Analysis type	other
Method	Miettinen & Nurminen
Parameter estimate	Difference in Percentage
Point estimate	2.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.6
upper limit	10.3

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 42 days after vaccination 1 and up to 42 days after vaccination 2 for all non-serious adverse events; Up to 180 days after vaccination 2 for all serious adverse events.

Adverse event reporting additional description:

The analysis population consisted of all randomized/allocated participants who received at least 1 dose of study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	VARIVAX (2016 CP) + M-M-R II

Reporting group description:

2016 Commercial Process vaccine 0.5 mL administered in the left arm or thigh and M-M-R® II vaccine 0.5 mL administered in the right arm or thigh by subcutaneous injection on Day 1 and Day 91.

Reporting group title	VARIVAX PE34 + M-M-R II

Reporting group description:

VARIVAX® Passage Extension 34 (PE34) Process 0.5 mL administered in the left arm and M-M-R®II vaccine 0.5 mL administered in the right arm by subcutaneous injection on Day 1 and Day 91.

Serious adverse events	VARIVAX (2016 CP) + M-M-R II	VARIVAX PE34 + M-M-R II	
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 300 (2.00%)	6 / 299 (2.01%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	1 / 300 (0.33%)	0 / 299 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Balanoposthitis			
subjects affected / exposed	0 / 300 (0.00%)	1 / 299 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Adenovirus infection			

subjects affected / exposed	0 / 300 (0.00%)	1 / 299 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 300 (0.33%)	0 / 299 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Croup infectious			
subjects affected / exposed	0 / 300 (0.00%)	1 / 299 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterovirus infection			
subjects affected / exposed	1 / 300 (0.33%)	0 / 299 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 300 (0.33%)	1 / 299 (0.33%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	0 / 300 (0.00%)	1 / 299 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngeal abscess			
subjects affected / exposed	0 / 300 (0.00%)	1 / 299 (0.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 300 (0.33%)	0 / 299 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus bronchiolitis			

subjects affected / exposed	0 / 300 (0.00%)	2 / 299 (0.67%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			
subjects affected / exposed	1 / 300 (0.33%)	0 / 299 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			
subjects affected / exposed	1 / 300 (0.33%)	0 / 299 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	VARIVAX (2016 CP) + M-M-R II	VARIVAX PE34 + M-M-R II	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	240 / 300 (80.00%)	255 / 299 (85.28%)	
General disorders and administration site conditions			
Injection site bruising			
subjects affected / exposed	16 / 300 (5.33%)	12 / 299 (4.01%)	
occurrences (all)	19	14	
Injection site erythema			
subjects affected / exposed	87 / 300 (29.00%)	85 / 299 (28.43%)	
occurrences (all)	157	158	
Injection site pain			
subjects affected / exposed	59 / 300 (19.67%)	55 / 299 (18.39%)	
occurrences (all)	125	129	
Injection site swelling			
subjects affected / exposed	43 / 300 (14.33%)	47 / 299 (15.72%)	
occurrences (all)	64	66	
Pyrexia			
subjects affected / exposed	75 / 300 (25.00%)	97 / 299 (32.44%)	
occurrences (all)	111	134	
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	65 / 300 (21.67%)	35 / 299 (11.71%)	
occurrences (all)	78	40	
Teething			
subjects affected / exposed	50 / 300 (16.67%)	27 / 299 (9.03%)	
occurrences (all)	63	34	
Vomiting			
subjects affected / exposed	42 / 300 (14.00%)	36 / 299 (12.04%)	
occurrences (all)	47	40	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	56 / 300 (18.67%)	53 / 299 (17.73%)	
occurrences (all)	68	66	
Nasal congestion			
subjects affected / exposed	20 / 300 (6.67%)	26 / 299 (8.70%)	
occurrences (all)	30	33	
Rhinorrhoea			
subjects affected / exposed	44 / 300 (14.67%)	48 / 299 (16.05%)	
occurrences (all)	50	76	
Skin and subcutaneous tissue disorders			
Dermatitis diaper			
subjects affected / exposed	33 / 300 (11.00%)	39 / 299 (13.04%)	
occurrences (all)	44	46	
Rash			
subjects affected / exposed	27 / 300 (9.00%)	25 / 299 (8.36%)	
occurrences (all)	37	38	
Psychiatric disorders			
Irritability			
subjects affected / exposed	51 / 300 (17.00%)	50 / 299 (16.72%)	
occurrences (all)	70	74	
Infections and infestations			
Hand-foot-and-mouth disease			
subjects affected / exposed	10 / 300 (3.33%)	17 / 299 (5.69%)	
occurrences (all)	10	18	
Nasopharyngitis			

subjects affected / exposed	44 / 300 (14.67%)	33 / 299 (11.04%)	
occurrences (all)	49	38	
Otitis media			
subjects affected / exposed	26 / 300 (8.67%)	35 / 299 (11.71%)	
occurrences (all)	29	41	
Otitis media acute			
subjects affected / exposed	27 / 300 (9.00%)	24 / 299 (8.03%)	
occurrences (all)	29	24	
Upper respiratory tract infection			
subjects affected / exposed	49 / 300 (16.33%)	37 / 299 (12.37%)	
occurrences (all)	58	41	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 November 2017	Serious adverse event time period was changed to ~180 days after vaccination 2 and unsolicited injection-site reactions up to 42 days after each vaccination was added as a safety parameter.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported