



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 standard deviation | 13.0 ± 1.4 | 13.2 ± 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)

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|-----------------|---|
| 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 ($\geq 5\text{gpELISA units/mL}$)

| | |
|-----------------|--|
| End point title | Percentage of Participants with Immunogenicity to Varicella Zoster Virus in Participants Initially Seropositive to Varicella Zoster Virus Antibody ($\geq 5\text{gpELISA units/mL}$) |
|-----------------|--|

End point description:

The percentage of participants with seropositive antibody titer (≥ 1.25 gpELISA 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 (≥ 1.25 gpELISA 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 (≥ 1.25 gpELISA 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 ≥ 1.25 gpELISA 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 (≥ 1.25 gpELISA 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