Clinical trial results:
Double blinded, randomized, Priorix®- and placebo-controlled, trial to evaluate the optimal dose of MV-CHIK vaccine (against Chikungunya virus) in regard to immunogenicity, safety and tolerability in healthy volunteers

Summary

EudraCT number	2015-004037-26
Trial protocol	DE AT
Global end of trial date	16 April 2018

Results information

Result version number	v2 (current)
This version publication date	10 November 2021
First version publication date	09 February 2020
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	MV-CHIK-202

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02861586
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Themis Bioscience GmbH
Sponsor organisation address	Muthgasse 11/2, Vienna, Austria, 1190
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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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	16 April 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 September 2017
Global end of trial reached?	Yes
Global end of trial date	16 April 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the immunogenicity and safety of MV-CHIK 28 days after primary immunization regime, comprising one or two vaccinations.

Protection of trial subjects:

Subjects' safety was an essential concern in this clinical study MV-CHIK-202 and was addressed in the clinical study protocol: -Physical examination: During each study visit subjects underwent a symptom-directed physical examination and the assessment of vital signs like systolic and diastolic blood pressure, pulse and body temperature, allowed to detect and record adverse conditions. -Post vaccination reactogenicity assessment: All subjects were observed for 1 hour after each vaccination in order to investigate local and systemic tolerability and to ensure the subjects wellbeing before discharge. -AEs: For general safety reasons, all subjects that at least received one vaccination were followed up for at least 28 days after the last vaccination. -Body temperature: All subjects received a thermometer and were asked to note their daily body temperature in a diary for 7 days after each vaccination to perceive side effects. -Subject diary: Solicited AEs were recorded by the subjects by checking the presence of listed symptoms in a subject's diary. The diary provided also space for noting unsolicited AEs and concomitant medication. This enabled the subjects to better remember AEs and the investigator to gather and assess AEs in more detail. -Laboratory parameters: were regularly measured to reveal clinically relevant lab values on hematology, blood chemistry, coagulation parameters and urinalysis. All lab results were evaluated carefully by the investigator to identify adverse conditions. -Safety stopping rules: An independent DSMB was installed to review safety information, and if necessary, to determine whether study or individual subject stopping rules have been met. -Data Safety Monitoring Board (DSMB): In close cooperation with the DSMB and the investigators the protection of study participants was assured.

Background therapy:

n.a.

Evidence for comparator:

Priorix® (Glaxo Smith Kline GSK) a measles, mumps, rubella vaccine was used as a control-vaccine because the contained attenuated Schwarz measles virus strain is the same strain, used as backbone in MV-CHIK.

Actual start date of recruitment	17 August 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Austria: 168
Country: Number of subjects enrolled	Germany: 95
Worldwide total number of subjects	263
EEA total number of subjects	263

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	263
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

First subject in, Austria: 17-Aug-2016 Last subject out, Austria: 11-Jan-2018 First subject in, Germany: 04-May-2017 Last subject out, Germany: 16-Apr-2018

Pre-assignment

Screening details:

To confirm the health status of volunteers the following data and parameters were assessed during screening: Medical/vacination history, physical examination, hematology, coagulation parameters, HIV, hepatitis B/C, urinalysis

Period 1

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

Blinding implementation details:

This study was conducted in a double-blind manner in regard to assignment to Treatment Groups A, B, C or D. An assignment to the measles booster groups M1 and M2 was apparent to both subject and study personnel, but the vaccination sequence was kept double-blind (allocation to M1 or to M2 was unknown). Vaccine was prepared by authorized unblinded personnel otherwise not involved in the conduct of the study. Ready prepared syringes were blinded.

Arms

Are arms mutually exclusive?	Yes
Arm title	Treatment Group A; MV-CHIK Low

Arm description:

Participants received i.m. vaccinations with MV-CHIK low dose (5x10E4 (± 0.5 log) TCID50 per 0.3 mL) on study day 0 and 28, placebo on day 196.

Arm type	Experimental
Investigational medicinal product name	Placebo NaCl 0.9%
Investigational medicinal product code	Placebo
Other name	Physiological saline solution
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Treatment group A received i.m. vaccinations with 0.3 ml MV-CHIK low dose on study day 0 and 28, and 0.3 ml placebo on day 196.

Investigational medicinal product name	MV-CHIK low dose 5x10E4 (± 0.5 log) TCID50/dose
Investigational medicinal product code	MV-CHIK
Other name	Chikungunya vaccine
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Treatment group A received i.m. vaccinations with 0.3 ml MV-CHIK low dose on study day 0 and 28, and 0.3 ml placebo on day 196.

Arm title	Treatment Group B; MV-CHIK Low

Arm description:

Participants received i.m. vaccinations with placebo on study day 0; MV-CHIK low dose (5x10E4 (± 0.5 log) TCID50 per 0.3 mL) on day 28 and MV-CHIK boosting dose on day 196.

Arm type	Experimental

Investigational medicinal product name	MV-CHIK low dose 5x10E4 (± 0.5 log) TCID50/ dose
Investigational medicinal product code	MV-CHIK
Other name	Chikungunya vaccine
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Group B subjects received i.m. vaccinations with 0.3 ml placebo on study day 0, and 0.3 ml MV-CHIK low dose on day 28 and on day 196.

Investigational medicinal product name	Placebo NaCl 0.9%
Investigational medicinal product code	Placebo
Other name	physiological saline solution
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Group B subjects received i.m. vaccinations with 0.3 ml placebo on study day 0, and 0.3 ml MV-CHIK low dose on day 28 and on day 196.

Arm title	Treatment Group C; MV-CHIK High

Arm description:

Participants received i.m. vaccinations with MV-CHIK high dose (5x10E5 (± 0.5 log) TCID50 per 0.3 mL) on study day 0 and 28, placebo on day 196.

Arm type	Experimental
Investigational medicinal product name	Placebo NaCl 0.9%
Investigational medicinal product code	Placebo
Other name	Physiological saline solution
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Group C received i.m. vaccinations with 0.3 ml MV-CHIK high dose on study day 0 and 28, and 0.3 ml placebo on day 196.

Investigational medicinal product name	MV-CHIK high dose 5x10E5 (± 0.5 log) TCID50/ dose
Investigational medicinal product code	MV-CHIK
Other name	Chikungunya vaccine
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Intranasal use

Dosage and administration details:

Group C received i.m. vaccinations with 0.3 ml MV-CHIK high dose on study day 0 and 28, and 0.3 ml placebo on day 196.

Arm title	Treatment Group D; MV-CHIK High

Arm description:

Participants received i.m. vaccinations with placebo on study day 0, MV-CHIK high dose (5x10E5 (± 0.5 log) TCID50 per 0.3 mL) on study day 28 and MV-CHIK boosting dose on day 196.

Arm type	Experimental
Investigational medicinal product name	Placebo NaCl 0.9%
Investigational medicinal product code	Placebo
Other name	Physiological saline solution
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Group D received i.m. vaccinations with 0.3 ml placebo on study day 0, and 0.3 ml MV-CHIK high dose on study day 28 and on day 196.

Investigational medicinal product name	MV-CHIK high dose 5x10E5 (± 0.5 log) TCID50/ dose
Investigational medicinal product code	MV-CHIK
Other name	Chikungunya vaccine

Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Intranasal use

Dosage and administration details:

Group D received i.m. vaccinations with 0.3 ml placebo on study day 0, and 0.3 ml MV-CHIK high dose on study day 28 and on day 196.

Arm title	Measles Booster Group 1

Arm description:

Participants received i.m. vaccinations with Priorix® on study day -28, MV-CHIK on day 0 and 28, and placebo on day 168 and 196.

Arm type	Experimental
Investigational medicinal product name	Priorix® measles, mumps rubella vaccine
Investigational medicinal product code	Priorix® controll vaccine
Other name	comperator
Pharmaceutical forms	Powder for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects of group M1 received the control vaccine (Priorix®) 28 days prior to two MV-CHIK vaccinations on day 0 and 28, followed by two placebo injections on day 168 and 196.

Arm title	Measles Booster Group 2

Arm description:

Participants received i.m. vaccinations with Priorix® on study day -28, placebo on day 0 and 28, and MV-CHIK on day 168 and 196.

Arm type	Experimental
Investigational medicinal product name	Priorix® measles, mumps, rubella vaccine
Investigational medicinal product code	Priorix®controll vaccine
Other name	comperator
Pharmaceutical forms	Powder and solvent for suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Group M2 received the control vaccine (Priorix®) 28 days prior to two placebo injections on day 0 and 28, followed by two MV-CHIK vaccinations on day 168 and 196.

Arm title	Treatment Group A/C; Priorix®

Arm description:

Participants received i.m. vaccinations with Priorix® on study day 0 and 28, and placebo on day 196.

Arm type	Active comparator
Investigational medicinal product name	Priorix® measles, mumps, rubella vaccine
Investigational medicinal product code	Priorix® control vaccine
Other name	comperator
Pharmaceutical forms	Powder and solution for solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Control Group CV1, A/C received i.m. vaccinations with Priorix® on study day 0 and 28, and placebo on day 196.

Investigational medicinal product name	Placebo NaCl 0.9%
Investigational medicinal product code	Placebo
Other name	Physiological saline solution
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Control Group CV1, A/C received i.m. vaccinations with Priorix® on study day 0 and 28, and placebo on day 196.

Arm title	Treatment Group B/D; Priorix®

Arm description:	
Participants received i.m. vaccinations with placebo on study day 0, Priorix® on day 28 and one boosting dose with Priorix® on day 196.	
Arm type	Active comparator
Investigational medicinal product name	Priorix® measles, mumps, rubella vaccine
Investigational medicinal product code	Priorix® control vaccine
Other name	comperator
Pharmaceutical forms	Powder and solvent for solution for injection/skin-prick test
Routes of administration	Intramuscular use
Dosage and administration details:	
Control Group CV2, B/D received i.m. vaccinations with placebo on study day 0, and Priorix® on day 28 and day 196.	
Investigational medicinal product name	Placebo NaCl 0.9%
Investigational medicinal product code	Placebo
Other name	Physiological saline solution
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use
Dosage and administration details:	
Control Group CV2, B/D received i.m. vaccinations with placebo on study day 0, and Priorix® on day 28 and day 196.	

Number of subjects in period 1	Treatment Group A; MV-CHIK Low	Treatment Group B; MV-CHIK Low	Treatment Group C; MV-CHIK High
Started	51	47	47
Completed	47	46	47
Not completed	4	1	0
Consent withdrawn by subject	1	-	-
Adverse event, non-fatal	-	-	-
Lost to follow-up	3	1	-

Number of subjects in period 1	Treatment Group D; MV-CHIK High	Measles Booster Group 1	Measles Booster Group 2
Started	50	18	16
Completed	45	17	16
Not completed	5	1	0
Consent withdrawn by subject	1	1	-
Adverse event, non-fatal	1	-	-
Lost to follow-up	3	-	-

Number of subjects in period 1	Treatment Group A/C; Priorix®	Treatment Group B/D; Priorix®
Started	18	16
Completed	15	16
Not completed	3	0
Consent withdrawn by subject	2	-
Adverse event, non-fatal	-	-
Lost to follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Treatment Group A; MV-CHIK Low
Reporting group description:	
Participants received i.m. vaccinations with MV-CHIK low dose (5x10E4 (± 0.5 log) TCID50 per 0.3 mL) on study day 0 and 28, placebo on day 196.	
Reporting group title	Treatment Group B; MV-CHIK Low
Reporting group description:	
Participants received i.m. vaccinations with placebo on study day 0; MV-CHIK low dose (5x10E4 (± 0.5 log) TCID50 per 0.3 mL) on day 28 and MV-CHIK boosting dose on day 196.	
Reporting group title	Treatment Group C; MV-CHIK High
Reporting group description:	
Participants received i.m. vaccinations with MV-CHIK high dose (5x10E5 (± 0.5 log) TCID50 per 0.3 mL) on study day 0 and 28, placebo on day 196.	
Reporting group title	Treatment Group D; MV-CHIK High
Reporting group description:	
Participants received i.m. vaccinations with placebo on study day 0, MV-CHIK high dose (5x10E5 (± 0.5 log) TCID50 per 0.3 mL) on study day 28 and MV-CHIK boosting dose on day 196.	
Reporting group title	Measles Booster Group 1
Reporting group description:	
Participants received i.m. vaccinations with Priorix® on study day -28, MV-CHIK on day 0 and 28, and placebo on day 168 and 196.	
Reporting group title	Measles Booster Group 2
Reporting group description:	
Participants received i.m. vaccinations with Priorix® on study day -28, placebo on day 0 and 28, and MV-CHIK on day 168 and 196.	
Reporting group title	Treatment Group A/C; Priorix®
Reporting group description:	
Participants received i.m. vaccinations with Priorix® on study day 0 and 28, and placebo on day 196.	
Reporting group title	Treatment Group B/D; Priorix®
Reporting group description:	
Participants received i.m. vaccinations with placebo on study day 0, Priorix® on day 28 and one boosting dose with Priorix® on day 196.	

Reporting group values	Treatment Group A; MV-CHIK Low	Treatment Group B; MV-CHIK Low	Treatment Group C; MV-CHIK High
Number of subjects	51	47	47
Age categorical			
Units:			
Age continuous			
Units: years			
arithmetic mean	31.4	32.7	35.1
standard deviation	± 10.13	± 10.53	± 12.32
Gender categorical			
Units: Subjects			
Female	27	29	24
Male	24	18	23

Reporting group values	Treatment Group D; MV-CHIK High	Measles Booster Group 1	Measles Booster Group 2

Number of subjects	50	18	16
Age categorical Units:			

Age continuous Units: years			
arithmetic mean	31.2	31.1	32.6
standard deviation	± 9.93	± 10.41	± 10.28
Gender categorical Units: Subjects			
Female	27	11	5
Male	23	7	11

Reporting group values	Treatment Group A/C; Priorix®	Treatment Group B/D; Priorix®	Total
Number of subjects	18	16	263
Age categorical Units:			

Age continuous Units: years			
arithmetic mean	32.2	33.6	
standard deviation	± 10.01	± 11.56	-
Gender categorical Units: Subjects			
Female	10	7	140
Male	8	9	123

End points

End points reporting groups

Reporting group title	Treatment Group A; MV-CHIK Low
Reporting group description:	
Participants received i.m. vaccinations with MV-CHIK low dose (5x10E4 (± 0.5 log) TCID50 per 0.3 mL) on study day 0 and 28, placebo on day 196.	
Reporting group title	Treatment Group B; MV-CHIK Low
Reporting group description:	
Participants received i.m. vaccinations with placebo on study day 0; MV-CHIK low dose (5x10E4 (± 0.5 log) TCID50 per 0.3 mL) on day 28 and MV-CHIK boosting dose on day 196.	
Reporting group title	Treatment Group C; MV-CHIK High
Reporting group description:	
Participants received i.m. vaccinations with MV-CHIK high dose (5x10E5 (± 0.5 log) TCID50 per 0.3 mL) on study day 0 and 28, placebo on day 196.	
Reporting group title	Treatment Group D; MV-CHIK High
Reporting group description:	
Participants received i.m. vaccinations with placebo on study day 0, MV-CHIK high dose (5x10E5 (± 0.5 log) TCID50 per 0.3 mL) on study day 28 and MV-CHIK boosting dose on day 196.	
Reporting group title	Measles Booster Group 1
Reporting group description:	
Participants received i.m. vaccinations with Priorix® on study day -28, MV-CHIK on day 0 and 28, and placebo on day 168 and 196.	
Reporting group title	Measles Booster Group 2
Reporting group description:	
Participants received i.m. vaccinations with Priorix® on study day -28, placebo on day 0 and 28, and MV-CHIK on day 168 and 196.	
Reporting group title	Treatment Group A/C; Priorix®
Reporting group description:	
Participants received i.m. vaccinations with Priorix® on study day 0 and 28, and placebo on day 196.	
Reporting group title	Treatment Group B/D; Priorix®
Reporting group description:	
Participants received i.m. vaccinations with placebo on study day 0, Priorix® on day 28 and one boosting dose with Priorix® on day 196.	
Subject analysis set title	Baseline measles titer percentile 0 to 25%
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants in Treatment Groups A, B, C, and D categorized according to baseline measles titer value.	
Subject analysis set title	Baseline measles titer percentile 25 to 50%
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants in Treatment Groups A, B, C, and D categorized according to baseline measles titer value.	
Subject analysis set title	Baseline measles titer percentile 50 to 75%
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants in Treatment Groups A, B, C, and D categorized according to baseline measles titer value.	
Subject analysis set title	Baseline measles titer percentile 75 to 100%
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants in Treatment Groups A, B, C, and D categorized according to baseline measles titer value.	

Primary: Functional Anti-chikungunya Antibody Titers on Day 56 (28 Days Post Immunisation) Confirmed by Plaque Reduction Neutralization Test (PRNT50)

End point title	Functional Anti-chikungunya Antibody Titers on Day 56 (28 Days Post Immunisation) Confirmed by Plaque Reduction Neutralization Test (PRNT50)

End point description:

Immunogenicity on day 56 confirmed by the presence of functional anti-chikungunya antibodies as determined by the plaque reduction neutralization test (PRNT50). This means immunogenicity 28 days after primary immunization regime, comprising one or two vaccinations. The Per-Protocol (PP) population was defined as the mITT population minus subjects with at least one major protocol deviation.

End point type	Primary

End point timeframe:

Study day 56 (28 days after one or two vaccinations depending on treatment group).

End point values	Treatment Group A; MV-CHIK Low	Treatment Group B; MV-CHIK Low	Treatment Group C; MV-CHIK High	Treatment Group D; MV-CHIK High
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	44	47	44
Units: Titer				
geometric mean (standard deviation)	50.2 (± 127.69)	12.9 (± 100.47)	174.8 (± 436.11)	33.6 (± 59.38)

End point values	Measles Booster Group 1	Measles Booster Group 2	Treatment Group A/C; Priorix®	Treatment Group B/D; Priorix®
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	15	16	16
Units: Titer				
geometric mean (standard deviation)	80.0 (± 233.80)	5.0 (± 0.00)	5.0 (± 0.00)	5.0 (± 0.00)

Statistical analyses

Statistical analysis title	Treatment Group A vs Treatment Group B

Statistical analysis description:

Analysis of variance was conducted with treatment group as a fixed factor.

Comparison groups	Treatment Group B; MV-CHIK Low v Treatment Group A; MV-CHIK Low
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [1]
Method	ANOVA
Parameter estimate	Geometric mean ratio
Point estimate	3.9

Confidence interval	
level	95 %
sides	2-sided
lower limit	2
upper limit	7.7
Variability estimate	Standard deviation

Notes:

[1] - Pairwise comparisons were adjusted for multiple tests according to Tukey-Kramer. The threshold for significance was 0.05.

Statistical analysis title	Treatment Group A vs Treatment Group C

Statistical analysis description:

Analysis of variance was conducted with treatment group as a fixed factor.

Comparison groups	Treatment Group A; MV-CHIK Low v Treatment Group C; MV-CHIK High
Number of subjects included in analysis	96
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [2]
Method	ANOVA
Parameter estimate	Geometric Mean Ratio
Point estimate	0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	0.6

Notes:

[2] - Pairwise comparisons were adjusted for multiple tests according to Tukey-Kramer. The threshold for significance was 0.05.

Statistical analysis title	Treatment Group A vs Treatment Group D

Statistical analysis description:

Analysis of variance was conducted with treatment group as a fixed factor.

Comparison groups	Treatment Group A; MV-CHIK Low v Treatment Group D; MV-CHIK High
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.06334 [3]
Method	ANOVA
Parameter estimate	Geometric Mean Ratio
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	3

Notes:

[3] - Pairwise comparisons were adjusted for multiple tests according to Tukey-Kramer. The threshold for significance was 0.05.

Statistical analysis title	Treatment Group A vs Measles Booster Group 1

Statistical analysis description:

Analysis of variance was conducted with treatment group as a fixed factor.

Comparison groups	Treatment Group A; MV-CHIK Low v Measles Booster Group 1
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8065 [4]
Method	ANOVA
Parameter estimate	Geometric Mean Ratio
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	1.6

Notes:

[4] - Pairwise comparisons were adjusted for multiple tests according to Tukey-Kramer. The threshold for significance was 0.05.

Statistical analysis title	Treatment Group A vs Measles Booster Group 2

Statistical analysis description:

Analysis of variance was conducted with treatment group as a fixed factor.

Comparison groups	Treatment Group A; MV-CHIK Low v Measles Booster Group 2
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [5]
Method	ANOVA
Parameter estimate	Geometric Mean Ratio
Point estimate	10
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.8
upper limit	26.6

Notes:

[5] - Pairwise comparisons were adjusted for multiple tests according to Tukey-Kramer. The threshold for significance was 0.05.

Statistical analysis title	Treatment Group A vs Treatment Group A/C

Statistical analysis description:

Analysis of variance was conducted with treatment group as a fixed factor.

Comparison groups	Treatment Group A; MV-CHIK Low v Treatment Group A/C; Priorix®
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [6]
Method	ANOVA
Parameter estimate	Geometric Mean Ratio
Point estimate	0.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.3

Notes:

[6] - Pairwise comparisons were adjusted for multiple tests according to Tukey-Kramer. The threshold for significance was 0.05.

Statistical analysis title	Treatment Group A vs Treatment Group B/D

Statistical analysis description:

Analysis of variance was conducted with treatment group as a fixed factor.

Comparison groups	Treatment Group A; MV-CHIK Low v Treatment Group B/D; Priorix®
Number of subjects included in analysis	65
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [7]
Method	ANOVA
Parameter estimate	Geometric Mean Ratio
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.3

Notes:

[7] - Pairwise comparisons were adjusted for multiple tests according to Tukey-Kramer. The threshold for significance was 0.05.

Statistical analysis title	Treatment Group B vs Treatment Group C

Statistical analysis description:

Analysis of variance was conducted with treatment group as a fixed factor.

Comparison groups	Treatment Group B; MV-CHIK Low v Treatment Group C; MV-CHIK High
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [8]
Method	ANOVA
Parameter estimate	Geometric Mean Ratio
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.1

Notes:

[8] - Pairwise comparisons were adjusted for multiple tests according to Tukey-Kramer. The threshold for significance was 0.05.

Statistical analysis title	Treatment Group B vs Treatment Group D

Statistical analysis description:

Analysis of variance was conducted with treatment group as a fixed factor.

Comparison groups	Treatment Group B; MV-CHIK Low v Treatment Group D; MV-CHIK High
Number of subjects included in analysis	88
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0011 [9]
Method	ANOVA
Parameter estimate	Geometric Mean Ratio
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	0.8

Notes:

[9] - Pairwise comparisons were adjusted for multiple tests according to Tukey-Kramer. The threshold for significance was 0.05.

Statistical analysis title	Treatment Group B vs Measles Booster Group 1

Statistical analysis description:

Analysis of variance was conducted with treatment group as a fixed factor.

Comparison groups	Treatment Group B; MV-CHIK Low v Measles Booster Group 1
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [10]
Method	ANOVA
Parameter estimate	Geometric Mean Ratio
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	0.4

Notes:

[10] - Pairwise comparisons were adjusted for multiple tests according to Tukey-Kramer. The threshold for significance was 0.05.

Statistical analysis title	Treatment Group B vs Measles Booster Group 2

Statistical analysis description:

Analysis of variance was conducted with treatment group as a fixed factor.

Comparison groups	Treatment Group B; MV-CHIK Low v Measles Booster Group 2
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0718 [11]
Method	ANOVA
Parameter estimate	Geometric Mean Ratio
Point estimate	2.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	6.9

Notes:

[11] - Pairwise comparisons were adjusted for multiple tests according to Tukey-Kramer. The threshold for significance was 0.05.

Statistical analysis title	Treatment Group B vs Treatment Group A/C

Statistical analysis description:

Analysis of variance was conducted with treatment group as a fixed factor.

Comparison groups	Treatment Group B; MV-CHIK Low v Treatment Group A/C; Priorix®
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0593 [12]
Method	ANOVA
Parameter estimate	Geometric Mean Ratio
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	1

Notes:

[12] - Pairwise comparisons were adjusted for multiple tests according to Tukey-Kramer. The threshold for significance was 0.05.

Statistical analysis title	Treatment Group B vs Treatment Group B/D

Statistical analysis description:

Analysis of variance was conducted with treatment group as a fixed factor.

Comparison groups	Treatment Group B; MV-CHIK Low v Treatment Group B/D; Priorix®
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0593 [13]
Method	ANOVA
Parameter estimate	Geometric Mean Ratio
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	1

Notes:

[13] - Pairwise comparisons were adjusted for multiple tests according to Tukey-Kramer. The threshold for significance was 0.05.

Statistical analysis title	Treatment Group C vs Treatment Group D

Statistical analysis description:

Analysis of variance was conducted with treatment group as a fixed factor.

Comparison groups	Treatment Group C; MV-CHIK High v Treatment Group D; MV-CHIK High
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [14]
Method	ANOVA
Parameter estimate	Geometric Mean Ratio
Point estimate	5.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.6
upper limit	10.4

Notes:

[14] - Pairwise comparisons were adjusted for multiple tests according to Tukey-Kramer. The threshold for significance was 0.05.

Statistical analysis title	Treatment Group C vs Measles Booster Group 1

Statistical analysis description:

Analysis of variance was conducted with treatment group as a fixed factor.

Comparison groups	Treatment Group C; MV-CHIK High v Measles Booster Group 1
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2005 [15]
Method	ANOVA
Parameter estimate	Geometric Mean Ratio
Point estimate	2.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	5.7

Notes:

[15] - Pairwise comparisons were adjusted for multiple tests according to Tukey-Kramer. The threshold for significance was 0.05.

Statistical analysis title	Treatment Group C vs Measles Booster Group 2

Statistical analysis description:

Analysis of variance was conducted with treatment group as a fixed factor.

Comparison groups	Treatment Group C; MV-CHIK High v Measles Booster Group 2
Number of subjects included in analysis	62
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [16]
Method	ANOVA
Parameter estimate	Geometric Mean Ratio
Point estimate	35

Confidence interval	
level	95 %
sides	2-sided
lower limit	13.1
upper limit	93.1

Notes:

[16] - Pairwise comparisons were adjusted for multiple tests according to Tukey-Kramer. The threshold for significance was 0.05.

Statistical analysis title	Treatment Group C vs Treatment Group A/C

Statistical analysis description:

Analysis of variance was conducted with treatment group as a fixed factor.

Comparison groups	Treatment Group C; MV-CHIK High v Treatment Group A/C; Priorix®
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [17]
Method	ANOVA
Parameter estimate	Geometric Mean Ratio
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.1

Notes:

[17] - Pairwise comparisons were adjusted for multiple tests according to Tukey-Kramer. The threshold for significance was 0.05.

Statistical analysis title	Treatment Group C vs Treatment Group B/D

Statistical analysis description:

Analysis of variance was conducted with treatment group as a fixed factor.

Comparison groups	Treatment Group C; MV-CHIK High v Treatment Group B/D; Priorix®
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [18]
Method	ANOVA
Parameter estimate	Geometric Mean Ratio
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.1

Notes:

[18] - Pairwise comparisons were adjusted for multiple tests according to Tukey-Kramer. The threshold for significance was 0.05.

Statistical analysis title	Treatment Group D vs Measles Booster Group 1

Statistical analysis description:

Analysis of variance was conducted with treatment group as a fixed factor.

Comparison groups	Treatment Group D; MV-CHIK High v Measles Booster Group 1
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1138 [19]
Method	ANOVA
Parameter estimate	Geometric Mean Ratio
Point estimate	0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	1.1

Notes:

[19] - Pairwise comparisons were adjusted for multiple tests according to Tukey-Kramer. The threshold for significance was 0.05.

Statistical analysis title	Treatment Group D vs Measles Booster Group 2

Statistical analysis description:

Analysis of variance was conducted with treatment group as a fixed factor.

Comparison groups	Treatment Group D; MV-CHIK High v Measles Booster Group 2
Number of subjects included in analysis	59
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.0001 [20]
Method	ANOVA
Parameter estimate	Geometric mean ratio
Point estimate	6.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.5
upper limit	18.1

Notes:

[20] - Pairwise comparisons were adjusted for multiple tests according to Tukey-Kramer. The threshold for significance was 0.05.

Statistical analysis title	Treatment Group D vs. Treatment Group A/C

Statistical analysis description:

Analysis of variance was conducted with treatment group as a fixed factor.

Comparison groups	Treatment Group D; MV-CHIK High v Treatment Group A/C; Priorix®
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.0001 [21]
Method	ANOVA
Parameter estimate	Geometric Mean Ratio
Point estimate	0.1

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	0.4

Notes:

[21] - Pairwise comparisons were adjusted for multiple tests according to Tukey-Kramer. The threshold for significance was 0.05.

Statistical analysis title	Treatment Group D vs Treatment Group B/D

Statistical analysis description:

Analysis of variance was conducted with treatment group as a fixed factor.

Comparison groups	Treatment Group D; MV-CHIK High v Treatment Group B/D; Priorix®
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.0001 [22]
Method	ANOVA
Parameter estimate	Geometric Mean Ratio
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	0.4

Notes:

[22] - Pairwise comparisons were adjusted for multiple tests according to Tukey-Kramer. The threshold for significance was 0.05.

Statistical analysis title	Measles Booster Group 1 vs Measles Booster Group 2

Statistical analysis description:

Analysis of variance was conducted with treatment group as a fixed factor.

Comparison groups	Measles Booster Group 1 v Measles Booster Group 2
Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.0001 [23]
Method	ANOVA
Parameter estimate	Geometric Mean Ratio
Point estimate	16
Confidence interval	
level	95 %
sides	2-sided
lower limit	4.9
upper limit	52.4

Notes:

[23] - Pairwise comparisons were adjusted for multiple tests according to Tukey-Kramer. The threshold for significance was 0.05.

Statistical analysis title	Measles Booster Group 1 vs Treatment Group A/C

Statistical analysis description:

Analysis of variance was conducted with treatment group as a fixed factor.

Comparison groups	Measles Booster Group 1 v Treatment Group A/C; Priorix®
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.0001 [24]
Method	ANOVA
Parameter estimate	Geometric Mean Ratio
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.2

Notes:

[24] - Pairwise comparisons were adjusted for multiple tests according to Tukey-Kramer. The threshold for significance was 0.05

Statistical analysis title	Measles Booster Group 1 vs Treatment Group B/D

Statistical analysis description:

Analysis of variance was conducted with treatment group as a fixed factor.

Comparison groups	Measles Booster Group 1 v Treatment Group B/D; Priorix®
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	< 0.0001 [25]
Method	ANOVA
Parameter estimate	Geometric Mean Ratio
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	0.2

Notes:

[25] - Pairwise comparisons were adjusted for multiple tests according to Tukey-Kramer. The threshold for significance was 0.05

Statistical analysis title	Measles Booster Group 2 vs Treatment Group A/C

Statistical analysis description:

Analysis of variance was conducted with treatment group as a fixed factor.

Comparison groups	Measles Booster Group 2 v Treatment Group A/C; Priorix®
Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 1 [26]
Method	ANOVA
Parameter estimate	Geometric Mean Ratio
Point estimate	1

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	3.3

Notes:

[26] - Pairwise comparisons were adjusted for multiple tests according to Tukey-Kramer. The threshold for significance was 0.05.

Statistical analysis title	Measles Booster Group 2 vs Treatment Group B/D

Statistical analysis description:

Analysis of variance was conducted with treatment group as a fixed factor.

Comparison groups	Measles Booster Group 2 v Treatment Group B/D; Priorix®
Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 1 [27]
Method	ANOVA
Parameter estimate	Geometric Mean Ratio
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	3.3

Notes:

[27] - Pairwise comparisons were adjusted for multiple tests according to Tukey-Kramer. The threshold for significance was 0.05.

Statistical analysis title	Treatment Group A/C vs Treatment Group B/D

Statistical analysis description:

Analysis of variance was conducted with treatment group as a fixed factor.

Comparison groups	Treatment Group A/C; Priorix® v Treatment Group B/D; Priorix®
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 1 [28]
Method	ANOVA
Parameter estimate	Geometric Mean Ratio
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	3.2

Notes:

[28] - Pairwise comparisons were adjusted for multiple tests according to Tukey-Kramer. The threshold for significance was 0.05.

Secondary: Functional Anti-Chikungunya Antibody Titers on Days 0, 28, 196 and 224 (M1/M2 Groups Day 168) Confirmed by Plaque Reduction Neutralization Test (PRNT50)

End point title	Functional Anti-Chikungunya Antibody Titers on Days 0, 28, 196 and 224 (M1/M2 Groups Day 168) Confirmed by Plaque Reduction Neutralization Test (PRNT50)

End point description:

Evaluation of immunogenicity on days 0, 28, 196 and 224; additionally, for group M1 and M2 on day 168 as confirmed by the presence of functional anti-chikungunya antibodies as determined by the plaque reduction neutralization test (PRNT50). Please note that for some timepoints testing has not been done. "Not done" cannot be entered but only numerical values. "9999" serves as indicator of a test which was not performed. The Per-Protocol (PP) population was defined as the mITT population minus subjects with at least one major protocol deviation.

End point type	Secondary

End point timeframe:

Baseline until study day 224

End point values	Treatment Group A; MV-CHIK Low	Treatment Group B; MV-CHIK Low	Treatment Group C; MV-CHIK High	Treatment Group D; MV-CHIK High
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	44	47	44
Units: Titer				
geometric mean (standard deviation)				
Day 0	5.1 (± 0.71)	5.3 (± 3.16)	5.0 (± 0.00)	5.0 (± 0.00)
Day 28	11.2 (± 63.40)	5.5 (± 3.82)	25.7 (± 52.22)	5.1 (± 0.75)
Day 168	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Day 196	13.5 (± 33.46)	6.4 (± 8.29)	38.8 (± 70.59)	16.5 (± 81.75)
Day 224	14.6 (± 37.87)	70.5 (± 174.57)	41.8 (± 105.55)	609.8 (± 949.70)

End point values	Measles Booster Group 1	Measles Booster Group 2	Treatment Group A/C; Priorix®	Treatment Group B/D; Priorix®
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	15	16	16
Units: Titer				
geometric mean (standard deviation)				
Day 0	5.0 (± 0.00)	5.0 (± 0.00)	5.0 (± 0.00)	5.0 (± 0.00)
Day 28	13.5 (± 40.52)	5.0 (± 0.00)	5.0 (± 0.00)	5.0 (± 0.00)
Day 168	28.9 (± 52.25)	5.0 (± 0.00)	9999 (± 9999)	9999 (± 9999)
Day 196	24.1 (± 106.25)	11.5 (± 26.04)	5.0 (± 0.00)	5.0 (± 0.00)
Day 224	18.3 (± 87.50)	66.5 (± 172.62)	5.0 (± 0.00)	5.0 (± 0.00)

Statistical analyses

No statistical analyses for this end point

Secondary: Measurement of Anti-measles Antibody Titer by Enzyme Linked

Immunosorbent Assay

End point title	Measurement of Anti-measles Antibody Titer by Enzyme Linked Immunosorbent Assay

End point description:

Measurement of anti-measles antibody titers on day 0, 28, and 56; additionally for group M1 and M2 on day -28 as determined by enzyme linked immunosorbent assay (ELISA). Please note that for some timepoints testing has not been done. "Not done" cannot be entered but only numerical values. "9999" should serve as indicator of a test which was not performed. The Per-Protocol (PP) population was defined as the mITT population minus subjects with at least one major protocol deviation.

End point type	Secondary

End point timeframe:

Baseline until study day 56

End point values	Treatment Group A; MV-CHIK Low	Treatment Group B; MV-CHIK Low	Treatment Group C; MV-CHIK High	Treatment Group D; MV-CHIK High
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	44	47	44
Units: Titer				
geometric mean (standard deviation)				
Day -28	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Day 0	456.2 (± 1398.54)	398.1 (± 1267.55)	495.0 (± 1181.36)	401.8 (± 1073.54)
Day 28	1509.4 (± 1360.83)	396.9 (± 1183.04)	2343.9 (± 1357.29)	492.1 (± 1227.24)
Day 56	1651.8 (± 1384.39)	1255.0 (± 1279.28)	2750.5 (± 1284.23)	2435.2 (± 1461.78)

End point values	Measles Booster Group 1	Measles Booster Group 2	Treatment Group A/C; Priorix®	Treatment Group B/D; Priorix®
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	15	16	16
Units: Titer				
geometric mean (standard deviation)				
Day -28	542.6 (± 1118.52)	304.5 (± 343.53)	9999 (± 9999)	9999 (± 9999)
Day 0	785.6 (± 1149.47)	645.9 (± 850.56)	693.9 (± 1307.42)	390.4 (± 1106.86)
Day 28	1761.5 (± 1578.85)	561.2 (± 385.36)	1200.6 (± 1129.77)	447.5 (± 1139.37)
Day 56	1825.2 (± 1459.93)	521.4 (± 455.37)	1129.4 (± 1168.63)	673.8 (± 917.52)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Solicited Local and Systemic Adverse Events

End point title	Number of Participants With Solicited Local and Systemic Adverse Events

End point description:

Evaluation of solicited local and systemic adverse events as recorded in the subjects' diaries for 7 days after each vaccination. As per the protocol, adverse events were analyzed per treatment group but were not assessed with respect to individual vaccinations. All safety analyses were based on the Safety Population, which included all subjects who received at least one vaccination.

End point type	Secondary

End point timeframe:

Solicited adverse events were recorded for 7 days after each vaccination

End point values	Treatment Group A; MV-CHIK Low	Treatment Group B; MV-CHIK Low	Treatment Group C; MV-CHIK High	Treatment Group D; MV-CHIK High
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	47	47	50
Units: Participants	35	32	37	41

End point values	Measles Booster Group 1	Measles Booster Group 2	Treatment Group A/C; Priorix®	Treatment Group B/D; Priorix®
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	16	18	16
Units: Participants	13	10	14	10

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants who experienced treatment emergent adverse events

End point title	Number of participants who experienced treatment emergent adverse events

End point description:

Evaluation of all treatment emergent adverse events (TEAEs) occurred throughout the clinical study. Clinically relevant abnormal safety laboratory values were recorded as TEAEs. As per the protocol, adverse events were analyzed per treatment group but were not assessed with respect to individual vaccinations. All safety analyses were based on the Safety Population, which included all subjects who received at least one vaccination.

End point type	Secondary

End point timeframe:

First vaccination until study day 224

End point values	Treatment Group A; MV-CHIK Low	Treatment Group B; MV-CHIK Low	Treatment Group C; MV-CHIK High	Treatment Group D; MV-CHIK High
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	51	47	47	50
Units: Participants				
TEAEs	29	27	22	18
Serious TEAEs	1	2	0	1
Severe TEAEs	1	2	0	2
Related TEAEs	8	11	4	10
Medically Attended TEAEs	12	15	9	8
TEAEs where an action was taken	0	1	0	1
TEAEs of special interest	2	2	0	1

End point values	Measles Booster Group 1	Measles Booster Group 2	Treatment Group A/C; Priorix®	Treatment Group B/D; Priorix®
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	18	16	18	16
Units: Participants				
TEAEs	11	9	10	7
Serious TEAEs	0	0	1	1
Severe TEAEs	1	1	1	0
Related TEAEs	4	5	2	1
Medically Attended TEAEs	4	3	3	1
TEAEs where an action was taken	0	0	0	1
TEAEs of special interest	2	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Shedding of Live Recombinant Virus in Urine Until Day 196

End point title	Number of Participants With Shedding of Live Recombinant Virus in Urine Until Day 196[29]

End point description:

Shedding was observed in a subset of subjects at one Austrian study site, by qualitative determination of live recombinant measles virus in urine by polymerase chain reaction (PCR). As subjects of the measles booster groups M1 and M2 received a measles vaccination prior to the modified MV-CHIK vaccine, these groups had to be excluded from measles shedding analysis.

End point type	Secondary

End point timeframe:

Baseline until study day 196; assessed on days 0, 7, 10, 14, 28 and 196

Notes:

[29] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistic calculations were planned or performed - not one case of sheeding was observed. Shedding analysis relies on PCR methods amplifying measles sequences. As M1 and M2

groups receive a measles vaccination and the study vaccination (modified measles virus), a potential positive result would not be indicative of the reason and therefore these groups were not tested for shedding.

End point values	Treatment Group A; MV-CHIK Low	Treatment Group B; MV-CHIK Low	Treatment Group C; MV-CHIK High	Treatment Group D; MV-CHIK High
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	4	8	5
Units: Participants				
Visit 1/Day 0	0	0	0	0
Day 7	0	0	0	0
Day 10	0	0	0	0
Day 14	0	0	0	0
Visit 2/Day 28	0	0	0	0
Visit 5/Day 196	0	0	0	0

End point values	Treatment Group A/C; Priorix®	Treatment Group B/D; Priorix®		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	2		
Units: Participants				
Visit 1/Day 0	0	0		
Day 7	0	0		
Day 10	0	0		
Day 14	0	0		
Visit 2/Day 28	0	0		
Visit 5/Day 196	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Shedding of Live Recombinant Virus in Saliva Until Day 196

End point title	Number of Participants With Shedding of Live Recombinant Virus in Saliva Until Day 196[30]

End point description:

Shedding was observed in a subset of subjects at one Austrian study site, by qualitative determination of live recombinant measles virus in saliva by polymerase chain reaction (PCR). As subjects of the measles booster groups M1 and M2 received a measles vaccination prior to the modified MV-CHIK vaccine, these groups had to be excluded from measles shedding analysis.

End point type	Secondary

End point timeframe:

Baseline until study day 196; assessed on days 0, 7, 10, 14, 28 and 196

Notes:

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

Justification: No statistic calculations were planned or performed - not one case of sheeding was observed. Shedding analysis relies on PCR methods amplifying measles sequences. As M1 and M2 groups receive a measles vaccination and the study vaccination (modified measles virus), a potential positive result would not be indicative of the reason and therefore these groups were not tested for shedding.

End point values	Treatment Group A; MV-CHIK Low	Treatment Group B; MV-CHIK Low	Treatment Group C; MV-CHIK High	Treatment Group D; MV-CHIK High
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	4	8	5
Units: Participants				
Visit 1/Day 0	0	0	0	0
Day 7	0	0	0	0
Day 10	0	0	0	0
Day 14	0	0	0	0
Visit 2/Day 28	0	0	0	0
Visit 5/Day 196	0	0	0	0

End point values	Treatment Group A/C; Priorix®	Treatment Group B/D; Priorix®		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4	2		
Units: Participants				
Visit 1/Day 0	0	0		
Day 7	0	0		
Day 10	0	0		
Day 14	0	0		
Visit 2/Day 28	0	0		
Visit 5/Day 196	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Chikungunya Virus Specific T Cell Responses

End point title	Chikungunya Virus Specific T Cell Responses

End point description:

Peripheral blood mononuclear cells (PBMCs) were isolated from whole blood to determine functional IL-2-producing T cells on day 0, 28, 56 and 224 in a subset of subjects. ELISpots were performed using peptides covering the CHIK proteins E1, E2 and C for re-stimulation, thereby producing three values per sample representing the number of spots per 1 x 10^6 PBMCs. If one or more of the three values was greater than 50, the sample was considered positive and the highest of the three values was used in the analysis. If all three values were below 50, the sample was considered negative and a value of 0.0 was used for analysis. Please note that for some timepoints testing has not been done. "Not done" cannot be entered but only numerical values. "9999" should serve as indicator of a test which was not performed. A subset of the mITT Population was analyzed for T-cell Response.

End point type	Secondary

End point timeframe:

Baseline until study day 224

End point values	Treatment Group A; MV-CHIK Low	Treatment Group B; MV-CHIK Low	Treatment Group C; MV-CHIK High	Treatment Group D; MV-CHIK High
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	15	12	14	11
Units: Titer				
arithmetic mean (standard deviation)				
Visit 1/Day 0	0.0 (± 0.00)	12.1 (± 40.10)	0.0 (± 0.00)	0.0 (± 0.00)
Visit 2/Day 28	41.5 (± 128.71)	9999 (± 9999)	10.5 (± 39.29)	9999 (± 9999)
Visit 3/Day 56	46.5 (± 63.54)	36.7 (± 68.44)	53.4 (± 74.83)	6.5 (± 21.41)
Visit 6/Day 224	28.3 (± 48.92)	71.8 (± 13.2)	11.6 (± 23.06)	30.1 (± 61.48)

End point values	Measles Booster Group 1	Measles Booster Group 2	Treatment Group A/C; Priorix®	Treatment Group B/D; Priorix®
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	4	5	5
Units: Titer				
arithmetic mean (standard deviation)				
Visit 1/Day 0	0.0 (± 0.00)	9999 (± 9999)	0.0 (± 0.00)	0.0 (± 0.00)
Visit 2/Day 28	9999 (± 9999)	9999 (± 9999)	0.0 (± 0.00)	9999 (± 9999)
Visit 3/Day 56	47.0 (± 51.55)	0.0 (± 0.00)	0.0 (± 0.00)	25.2 (± 56.35)
Visit 6/Day 224	0.0 (± 0.00)	0.0 (± 0.00)	0.0 (± 0.00)	13.2 (± 29.52)

Statistical analyses

No statistical analyses for this end point

Secondary: Immunogenicity confirmed by the presence of humoral anti-chikungunya antibodies, determined by enzyme linked immunosorbent assay (ELISA)

End point title	Immunogenicity confirmed by the presence of humoral anti-chikungunya antibodies, determined by enzyme linked immunosorbent assay (ELISA)

End point description:

Evaluation of immunogenicity mediated by serum IgG antibodies against Chikungunya on days 0, 28, 196 and 224; additionally for group M1 and M2 on day 168, determined by enzyme linked immunosorbent assay (ELISA). Please note that for some timepoints testing has not been done. "Not done" cannot be entered but only numerical values. "9999" should serve as indicator of a test which was not performed. The Per-Protocol (PP) population was defined as the mITT population minus subjects with at least one major protocol Deviation.

End point type	Secondary

End point timeframe:

Baseline until study day 224; assessed on days 0, 28, 168, 196 and 224

End point values	Treatment Group A; MV-CHIK Low	Treatment Group B; MV-CHIK Low	Treatment Group C; MV-CHIK High	Treatment Group D; MV-CHIK High
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	49	44	47	44
Units: Titer				
geometric mean (standard deviation)				
Visit 1/Day 0	2.1 (± 1.94)	2.3 (± 1.68)	2.3 (± 2.75)	2.2 (± 1.53)
Visit 2/Day 28	3.2 (± 6.57)	2.2 (± 1.81)	6.2 (± 4.65)	2.5 (± 1.74)
Visit 3/Day 56	13.6 (± 31.84)	3.4 (± 6.26)	74.4 (± 41.45)	6.6 (± 18.68)
Visit 4/Day 168	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)	9999 (± 9999)
Visit 5/Day 196	5.6 (± 3.0)	3.0 (± 3.11)	15.2 (± 25.08)	5.6 (± 21.33)
Visit 6/Day 224	4.6 (± 9.46)	25.4 (± 52.43)	13.1 (± 24.24)	130.8 (± 43.94)

End point values	Measles Booster Group 1	Measles Booster Group 2	Treatment Group A/C; Priorix®	Treatment Group B/D; Priorix®
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	16	15	16	16
Units: Titer				
geometric mean (standard deviation)				
Visit 1/Day 0	2.4 (± 2.69)	2.2 (± 2.25)	3.6 (± 3.64)	1.7 (± 1.05)
Visit 2/Day 28	4.3 (± 9.48)	2.0 (± 2.37)	3.4 (± 3.13)	2.0 (± 2.75)
Visit 3/Day 56	28.0 (± 47.51)	2.3 (± 2.10)	3.4 (± 4.06)	1.7 (± 1.63)
Visit 4/Day 168	9.5 (± 29.82)	1.8 (± 2.28)	9999 (± 9999)	9999 (± 9999)
Visit 5/Day 196	8.9 (± 24.13)	3.6 (± 5.48)	3.3 (± 4.02)	1.9 (± 2.06)
Visit 6/Day 224	7.3 (± 28.56)	20.4 (± 43.19)	3.1 (± 4.66)	1.7 (± 1.82)

Statistical analyses

No statistical analyses for this end point

Secondary: Functional anti-chikungunya antibody titers on day 56 (28 days post immunization) by baseline measles titer

End point title	Functional anti-chikungunya antibody titers on day 56 (28 days post immunization) by baseline measles titer

End point description:

To determine the potential impact of pre-existing antibodies against measles on MV-CHIK immunogenicity, participants from treatment Groups A to D were divided into quartiles according to serum IgG concentrations against measles virus on Day 0. Functional anti-chikungunya antibodies as determined by PRNT50 were compared between groups. The Per-Protocol (PP) population was defined as the mITT population minus subjects with at least one major protocol Deviation.

End point type	Secondary

End point timeframe:

Study day 56 (28 days after one or two vaccinations depending on treatment group)

End point values	Baseline measles titer percentile 0 to 25%	Baseline measles titer percentile 25 to 50%	Baseline measles titer percentile 50 to 75%	Baseline measles titer percentile 75 to 100%
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	45	48	45	46
Units: Titer				
geometric mean (standard deviation)	155.1 (± 532.68)	177.0 (± 897.74)	117.6 (± 346.86)	100.8 (± 535.78)

Statistical analyses

Statistical analysis title	0 to 25% vs. 25 to 50%
Statistical analysis description:	
Analysis of variance was performed with baseline measles titer group as a fixed factor.	
Comparison groups	Baseline measles titer percentile 25 to 50% v Baseline measles titer percentile 0 to 25%
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9775
Method	ANOVA
Parameter estimate	Geometric mean ratio
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	2

Statistical analysis title	0 to 25% vs 50 to 75%
Statistical analysis description:	
Analysis of variance was performed with baseline measles titer group as a fixed factor.	
Comparison groups	Baseline measles titer percentile 0 to 25% v Baseline measles titer percentile 50 to 75%
Number of subjects included in analysis	90
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8366
Method	ANOVA
Parameter estimate	Geometric mean ratio
Point estimate	1.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	3.1

Statistical analysis title	0 to 25% vs 75 to 100%
Statistical analysis description:	
Analysis of variance was performed with baseline measles titer group as a fixed factor.	
Comparison groups	Baseline measles titer percentile 0 to 25% v Baseline measles titer percentile 75 to 100%
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5625
Method	ANOVA
Parameter estimate	Geometric mean ratio
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	3.6

Statistical analysis title	25 to 50% vs 50 to 75%
Statistical analysis description:	
Analysis of variance was performed with baseline measles titer group as a fixed factor.	
Comparison groups	Baseline measles titer percentile 25 to 50% v Baseline measles titer percentile 50 to 75%
Number of subjects included in analysis	93
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5924
Method	ANOVA
Parameter estimate	Geometric mean ratio
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	3.5

Statistical analysis title	25 to 50% vs 75 to 100%

Statistical analysis description:

Analysis of variance was performed with baseline measles titer group as a fixed factor.

Comparison groups	Baseline measles titer percentile 25 to 50% v Baseline measles titer percentile 75 to 100%
Number of subjects included in analysis	94
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3122
Method	ANOVA
Parameter estimate	Geometric mean ratio
Point estimate	1.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.8
upper limit	4.1

Statistical analysis title	50 to 75% vs 75 to 100%

Statistical analysis description:

Analysis of variance was performed with baseline measles titer group as a fixed factor.

Comparison groups	Baseline measles titer percentile 50 to 75% v Baseline measles titer percentile 75 to 100%
Number of subjects included in analysis	91
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9665
Method	ANOVA
Parameter estimate	Geometric mean ratio
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	2.8

Adverse events

Adverse events information

Timeframe for reporting adverse events:

32 - 36 weeks; Adverse events were collected in the period after the first vaccination until the last on site study visit.

Adverse event reporting additional description:

Local and systemic solicited adverse events were collected via subject diary, for 7 days after each vaccination. As per the protocol, adverse events were analyzed per treatment group but were not assessed with respect to individual vaccinations.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups

Reporting group title	Treatment Group A

Reporting group description:

Participants received i.m. vaccinations with MV-CHIK low dose (5xE4 (± 0.5 log) TCID50 per 0.3 mL) on study day 0 and 28, placebo on day 196.

Reporting group title	Treatment Group C

Reporting group description:

Participants received i.m. vaccinations with MV-CHIK high dose (5xE5 (± 0.5 log) TCID50 per 0.3 mL) on study day 0 and 28, placebo on day 196.

Reporting group title	Treatment Group B

Reporting group description:

Participants received i.m. vaccinations with placebo on study day 0. MV-CHIK low dose (5xE4 (± 0.5 log) TCID50 per 0.3 mL) on day 28 and MV-CHIK boosting dose on day 196.

Reporting group title	Treatment Group D

Reporting group description:

Participants received i.m. vaccinations with placebo on study day 0, MV-CHIK high dose (5xE5 (± 0.5 log) TCID50 per 0.3 mL) on study day 28 and MV-CHIK boosting dose on day 196.

Reporting group title	Treatment Group M1

Reporting group description:

Participants received i.m. vaccinations with Priorix® on study day -28, MV-CHIK on day 0 and 28 and placebo on day 168 and 196.

Reporting group title	Treatment Group M2

Reporting group description:

Participants received i.m. vaccinations with Priorix® on study day -28, placebo on day 0 and 28 and MV-CHIK on day 168 and 196.

Reporting group title	Control Group CV1, A/C

Reporting group description:

Participants received i.m. vaccinations with Priorix® on study day 0 and 28, placebo on day 196.

Reporting group title	Control Group CV2, B/D

Reporting group description:

Participants received i.m. vaccinations with placebo on study day 0, Priorix® on day 28 and one boosting dose with Priorix® on day 196.

Serious adverse events	Treatment Group A	Treatment Group C	Treatment Group B
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 51 (1.96%)	0 / 47 (0.00%)	2 / 47 (4.26%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Laryngeal cancer			
subjects affected / exposed	0 / 51 (0.00%)	0 / 47 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Papillary thyroid cancer			
subjects affected / exposed	0 / 51 (0.00%)	0 / 47 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ligament rupture			
subjects affected / exposed	0 / 51 (0.00%)	0 / 47 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion			
subjects affected / exposed	0 / 51 (0.00%)	0 / 47 (0.00%)	1 / 47 (2.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Umbilical hernia			
subjects affected / exposed	1 / 51 (1.96%)	0 / 47 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 51 (0.00%)	0 / 47 (0.00%)	0 / 47 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Treatment Group D	Treatment Group M1	Treatment Group M2
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 50 (2.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Laryngeal cancer			
subjects affected / exposed	0 / 50 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Papillary thyroid cancer			
subjects affected / exposed	1 / 50 (2.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ligament rupture			
subjects affected / exposed	0 / 50 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion			
subjects affected / exposed	0 / 50 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Umbilical hernia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 50 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Control Group CV1, A/C	Control Group CV2, B/D	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 18 (5.56%)	1 / 16 (6.25%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Laryngeal cancer			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Papillary thyroid cancer			
subjects affected / exposed	0 / 18 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Ligament rupture			
subjects affected / exposed	0 / 18 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion			
subjects affected / exposed	0 / 18 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Umbilical hernia			
subjects affected / exposed	0 / 18 (0.00%)	0 / 16 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 18 (0.00%)	1 / 16 (6.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Treatment Group A	Treatment Group C	Treatment Group B
Total subjects affected by non-serious adverse events			
subjects affected / exposed	40 / 51 (78.43%)	38 / 47 (80.85%)	36 / 47 (76.60%)
Vascular disorders			
Haematoma			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 47 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	13 / 51 (25.49%)	9 / 47 (19.15%)	9 / 47 (19.15%)
occurrences (all)	17	12	12
Fatigue			
subjects affected / exposed	10 / 51 (19.61%)	13 / 47 (27.66%)	9 / 47 (19.15%)
occurrences (all)	15	19	20
Axillary pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 47 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Injection site erythema			
subjects affected / exposed	6 / 51 (11.76%)	10 / 47 (21.28%)	5 / 47 (10.64%)
occurrences (all)	8	18	6
Injection site induration			
subjects affected / exposed	5 / 51 (9.80%)	8 / 47 (17.02%)	6 / 47 (12.77%)
occurrences (all)	7	12	6
Injection site oedema			
subjects affected / exposed	4 / 51 (7.84%)	3 / 47 (6.38%)	2 / 47 (4.26%)
occurrences (all)	8	4	2
Injection site pain			

subjects affected / exposed	24 / 51 (47.06%)	30 / 47 (63.83%)	21 / 47 (44.68%)
occurrences (all)	51	71	37
Injection site pruritus			
subjects affected / exposed	0 / 51 (0.00%)	2 / 47 (4.26%)	1 / 47 (2.13%)
occurrences (all)	0	4	1
Pyrexia			
subjects affected / exposed	3 / 51 (5.88%)	0 / 47 (0.00%)	1 / 47 (2.13%)
occurrences (all)	3	0	1
Immune system disorders			
Seasonal allergy			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 47 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Dysmenorrhoea			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 51 (1.96%)	1 / 47 (2.13%)	1 / 47 (2.13%)
occurrences (all)	2	2	3
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 51 (1.96%)	4 / 47 (8.51%)	1 / 47 (2.13%)
occurrences (all)	1	5	1
Cough			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 51 (1.96%)	1 / 47 (2.13%)	2 / 47 (4.26%)
occurrences (all)	1	1	2
Dysphonia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 51 (0.00%)	1 / 47 (2.13%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Sneezing			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 51 (0.00%)	0 / 47 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Injury			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 51 (0.00%)	1 / 47 (2.13%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Skin abrasion			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 47 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Contusion			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 47 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	20 / 51 (39.22%)	14 / 47 (29.79%)	16 / 47 (34.04%)
occurrences (all)	36	30	32
Blood and lymphatic system disorders			
Lymphadenopathy			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 51 (3.92%)	0 / 47 (0.00%)	0 / 47 (0.00%)
occurrences (all)	2	0	0
Ear and labyrinth disorders			
Ear pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 51 (0.00%)	1 / 47 (2.13%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Vertigo			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 47 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Eye disorders			

Dry eye			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 47 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Eye pruritus			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 47 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal pain upper			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 51 (5.88%)	2 / 47 (4.26%)	0 / 47 (0.00%)
occurrences (all)	3	2	0
Diarrhoea			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 51 (1.96%)	0 / 47 (0.00%)	1 / 47 (2.13%)
occurrences (all)	1	0	1
Abdominal pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 51 (1.96%)	0 / 47 (0.00%)	1 / 47 (2.13%)
occurrences (all)	1	0	1
Toothache			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 51 (1.96%)	0 / 47 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	8 / 51 (15.69%)	2 / 47 (4.26%)	2 / 47 (4.26%)
occurrences (all)	10	2	3
Vomiting			
subjects affected / exposed	0 / 51 (0.00%)	1 / 47 (2.13%)	0 / 47 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Dermatitis contact			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 51 (1.96%)	0 / 47 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	0 / 51 (0.00%)	0 / 47 (0.00%)	3 / 47 (6.38%)
occurrences (all)	0	0	3
Erythema multiforme			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 47 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Hypertonic bladder			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 47 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 51 (3.92%)	2 / 47 (4.26%)	2 / 47 (4.26%)
occurrences (all)	2	3	2
Myalgia			
subjects affected / exposed	9 / 51 (17.65%)	5 / 47 (10.64%)	6 / 47 (12.77%)
occurrences (all)	12	7	9
Musculoskeletal pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 47 (0.00%)	1 / 47 (2.13%)
occurrences (all)	0	0	1
Bursitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 47 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 47 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Arthralgia			

subjects affected / exposed	8 / 51 (15.69%)	2 / 47 (4.26%)	5 / 47 (10.64%)
occurrences (all)	9	2	7
Arthritis reactive			
subjects affected / exposed	0 / 51 (0.00%)	0 / 47 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Intervertabral disc protrustion			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 51 (0.00%)	1 / 47 (2.13%)	0 / 47 (0.00%)
occurrences (all)	0	2	0
Limb discomfort			
subjects affected / exposed	7 / 51 (13.73%)	4 / 47 (8.51%)	5 / 47 (10.64%)
occurrences (all)	7	4	7
Infections and infestations			
Nasopharyngitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	7 / 51 (13.73%)	4 / 47 (8.51%)	4 / 47 (8.51%)
occurrences (all)	7	5	4
Rhinitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 51 (3.92%)	3 / 47 (6.38%)	0 / 47 (0.00%)
occurrences (all)	2	3	0
Upper respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 51 (5.88%)	1 / 47 (2.13%)	3 / 47 (6.38%)
occurrences (all)	3	2	4
Urinary tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 51 (1.96%)	1 / 47 (2.13%)	1 / 47 (2.13%)
occurrences (all)	1	1	1
Gingivitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 47 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Hordeolum			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 51 (0.00%)	0 / 47 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 47 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Vaginal infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 47 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Vulvovaginal candidiasis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 47 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Cystitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 47 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 51 (0.00%)	0 / 47 (0.00%)	2 / 47 (4.26%)
occurrences (all)	0	0	2
Otitis externa			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 51 (1.96%)	0 / 47 (0.00%)	0 / 47 (0.00%)
occurrences (all)	1	0	0
Tonsillitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 51 (0.00%)	1 / 47 (2.13%)	1 / 47 (2.13%)
occurrences (all)	0	1	1
Metabolism and nutrition disorders			
Appetite disorder			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 51 (0.00%)	0 / 47 (0.00%)	0 / 47 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Treatment Group D	Treatment Group M1	Treatment Group M2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	41 / 50 (82.00%)	15 / 18 (83.33%)	14 / 16 (87.50%)
Vascular disorders			
Haematoma			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	8 / 50 (16.00%)	2 / 18 (11.11%)	4 / 16 (25.00%)
occurrences (all)	16	2	7
Fatigue			
subjects affected / exposed	14 / 50 (28.00%)	5 / 18 (27.78%)	4 / 16 (25.00%)
occurrences (all)	25	10	9
Axillary pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Injection site erythema			
subjects affected / exposed	9 / 50 (18.00%)	2 / 18 (11.11%)	2 / 16 (12.50%)
occurrences (all)	11	4	2
Injection site induration			
subjects affected / exposed	15 / 50 (30.00%)	2 / 18 (11.11%)	1 / 16 (6.25%)
occurrences (all)	24	2	1
Injection site oedema			
subjects affected / exposed	4 / 50 (8.00%)	1 / 18 (5.56%)	1 / 16 (6.25%)
occurrences (all)	6	2	1
Injection site pain			
subjects affected / exposed	39 / 50 (78.00%)	8 / 18 (44.44%)	7 / 16 (43.75%)
occurrences (all)	119	29	18
Injection site pruritus			

subjects affected / exposed	3 / 50 (6.00%)	0 / 18 (0.00%)	2 / 16 (12.50%)
occurrences (all)	4	0	2
Pyrexia			
subjects affected / exposed	0 / 50 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Immune system disorders			
Seasonal allergy			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 50 (2.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	2	1	0
Reproductive system and breast disorders			
Dysmenorrhoea			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 50 (4.00%)	2 / 18 (11.11%)	1 / 16 (6.25%)
occurrences (all)	8	4	1
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 50 (2.00%)	2 / 18 (11.11%)	1 / 16 (6.25%)
occurrences (all)	1	3	1
Cough			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	1 / 18 (5.56%)	1 / 16 (6.25%)
occurrences (all)	0	1	1
Dysphonia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Sneezing			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			

Injury			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 50 (2.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Contusion			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Headache			
subjects affected / exposed	17 / 50 (34.00%)	9 / 18 (50.00%)	8 / 16 (50.00%)
occurrences (all)	47	18	19
Blood and lymphatic system disorders			
Lymphadenopathy			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	3	0
Vertigo			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 18 (0.00%)	2 / 16 (12.50%)
occurrences (all)	0	0	2
Eye disorders			
Dry eye			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Eye pruritus			

alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal pain upper			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 50 (2.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	1	1	0
Abdominal pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	2
Toothache			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 50 (2.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Nausea			
subjects affected / exposed	6 / 50 (12.00%)	2 / 18 (11.11%)	1 / 16 (6.25%)
occurrences (all)	7	2	3
Vomiting			
subjects affected / exposed	1 / 50 (2.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Dermatitis contact			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 50 (2.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	1	0	0
Rash			
subjects affected / exposed	1 / 50 (2.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	8	1	0
Erythema multiforme			

alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Renal and urinary disorders			
Hypertonic bladder			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	13 / 50 (26.00%)	4 / 18 (22.22%)	1 / 16 (6.25%)
occurrences (all)	22	8	2
Musculoskeletal pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Bursitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Arthralgia			
subjects affected / exposed	7 / 50 (14.00%)	2 / 18 (11.11%)	3 / 16 (18.75%)
occurrences (all)	11	3	3
Arthritis reactive			
subjects affected / exposed	0 / 50 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Intervertabral disc protrustion			

alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Limb discomfort			
subjects affected / exposed	11 / 50 (22.00%)	1 / 18 (5.56%)	1 / 16 (6.25%)
occurrences (all)	19	1	1
Infections and infestations			
Nasopharyngitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	4 / 50 (8.00%)	2 / 18 (11.11%)	1 / 16 (6.25%)
occurrences (all)	5	5	1
Rhinitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 50 (4.00%)	2 / 18 (11.11%)	2 / 16 (12.50%)
occurrences (all)	2	3	2
Upper respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 18 (0.00%)	0 / 16 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Hordeolum			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Respiratory tract infection			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 50 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Vaginal infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Vulvovaginal candidiasis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Cystitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 50 (2.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	1	0	1
Gastroenteritis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Otitis externa			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	1	0
Tonsillitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	0 / 18 (0.00%)	1 / 16 (6.25%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Appetite disorder			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 50 (0.00%)	1 / 18 (5.56%)	0 / 16 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	Control Group CV1, A/C	Control Group CV2, B/D	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 18 (77.78%)	11 / 16 (68.75%)	

Vascular disorders			
Haematoma			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 18 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Influenza like illness			
subjects affected / exposed	4 / 18 (22.22%)	1 / 16 (6.25%)	
occurrences (all)	4	1	
Fatigue			
subjects affected / exposed	5 / 18 (27.78%)	3 / 16 (18.75%)	
occurrences (all)	9	5	
Axillary pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 18 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Injection site erythema			
subjects affected / exposed	2 / 18 (11.11%)	2 / 16 (12.50%)	
occurrences (all)	3	2	
Injection site induration			
subjects affected / exposed	0 / 18 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Injection site oedema			
subjects affected / exposed	0 / 18 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Injection site pain			
subjects affected / exposed	6 / 18 (33.33%)	5 / 16 (31.25%)	
occurrences (all)	12	7	
Injection site pruritus			
subjects affected / exposed	0 / 18 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Pyrexia			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			

Seasonal allergy			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 18 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Reproductive system and breast disorders			
Dysmenorrhoea			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 18 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 18 (5.56%)	1 / 16 (6.25%)	
occurrences (all)	1	1	
Cough			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Dysphonia			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Sneezing			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Injury			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 18 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Skin abrasion			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Contusion			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 18 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Nervous system disorders			
Headache			
subjects affected / exposed	10 / 18 (55.56%)	6 / 16 (37.50%)	
occurrences (all)	19	13	
Blood and lymphatic system disorders			
Lymphadenopathy			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Ear and labyrinth disorders			
Ear pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 18 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Vertigo			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 18 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Dry eye			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 18 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Eye pruritus			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 18 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Abdominal pain upper			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 18 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Diarrhoea			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Abdominal pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Toothache			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	4 / 18 (22.22%)	2 / 16 (12.50%)	
occurrences (all)	7	2	
Vomiting			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Dermatitis contact			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	
occurrences (all)	2	0	
Rash			
subjects affected / exposed	2 / 18 (11.11%)	0 / 16 (0.00%)	
occurrences (all)	2	0	
Erythema multiforme			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 18 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Renal and urinary disorders			
Hypertonic bladder			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Back pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 18 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Myalgia			
subjects affected / exposed	5 / 18 (27.78%)	2 / 16 (12.50%)	
occurrences (all)	8	2	
Musculoskeletal pain			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Bursitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 18 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Muscle spasms			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 18 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Arthralgia			
subjects affected / exposed	3 / 18 (16.67%)	2 / 16 (12.50%)	
occurrences (all)	3	2	
Arthritis reactive			
subjects affected / exposed	0 / 18 (0.00%)	1 / 16 (6.25%)	
occurrences (all)	0	1	
Intervertabral disc protrustion			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Limb discomfort			

subjects affected / exposed	3 / 18 (16.67%)	2 / 16 (12.50%)	
occurrences (all)	3	2	
Infections and infestations			
Nasopharyngitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	2 / 18 (11.11%)	2 / 16 (12.50%)	
occurrences (all)	2	3	
Rhinitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 18 (5.56%)	0 / 16 (0.00%)	
occurrences (all)	1	0	
Gingivitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 18 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Hordeolum			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 18 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 18 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Vaginal infection			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 18 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Vulvovaginal candidiasis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 18 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Cystitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 18 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Gastroenteritis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 18 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Otitis externa			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 18 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Tonsillitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 18 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Appetite disorder			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 18 (0.00%)	0 / 16 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 August 2016	Protocol Amendment 1 (substantial, dated 26-Apr-2016) incorporated in Protocol version 1.3 (26-Apr-2016) before the first study submission. The protocol was amended: To precisely define the primary endpoint as immunogenicity on Day 56 for all treatment groups To adapt the study design (by shifting study visits) to enable immunogenicity measurements on Day 56 for all treatment groups To change the definition from three cohorts consisting of two different treatment regimens each, to a more reasonable definition of six treatment groups To define the dates of study visits based on an interval of 28 days and to rename the study days as follows: Screening Visit on Study Day -35; Visit 0 on Study Day -28; Visit 1 on Study Day 0; Visit 2 on Study Day 28; Visit 3 on Study Day 56; Visit 4 on Study Day 168; Visit 5 on Study Day 196; Visit 6 on Study Day 224 To state the study objectives more precisely To include a preliminary data analysis To describe the role of the DSMB To remove the safety assessment by telephone call, 12 months after the first vaccination To clarify that the control-vaccine Priorix® can be exchanged by MMR-Vax-Pro® or equal measles vaccine In addition, to correct typos, include some formal changes and update the list of abbreviations

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported