Clinical trial results:
Efficacy of MVA-NP+M1 in the influenza H3N2 Human Challenge model

Summary

EudraCT number	2018-004015-49
Trial protocol	BE
Global end of trial date	17 April 2020

Results information

Result version number	v1 (current)
This version publication date	23 December 2020
First version publication date	23 December 2020

Trial information

Trial identification

Sponsor protocol code	FLU010

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03883113
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Vaccitech Ltd
Sponsor organisation address	The Schrödinger Building, Heatley Road, The Oxford Science Park, Oxford, United Kingdom, OX4 4GE
Public contact	Chris Ellis, Vaccitech Ltd, enquiries@vaccitech.co.uk
Scientific contact	Tom Evans, MD, Vaccitech Ltd, tom.evans@vaccitech.co.uk

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	17 April 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 April 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to show that MVA-NP+M1 decreases the viral shedding of influenza virus, as measured by the cumulative area under the curve, following human challenge.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) Note for Guidance on Good Clinical Practice (GCP) (CPMP/ICH/135/95) and with applicable local requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 May 2019
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	6 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 145
Worldwide total number of subjects	145
EEA total number of subjects	145

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)	145
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at the SGS Clinical Pharmacology Unit in Antwerp, Belgium

Pre-assignment

Screening details:

Eight-hundred and nineteen (819) subjects were screened. One hundred and forty-five (145) subjects were actually enrolled and vaccinated.
The study consisted of an outpatient vaccination phase and at least 6 weeks later an inpatient challenge phase.

Period 1

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

Blinding implementation details:

Since MVA-NP+M1 has a cloudy appearance compared to saline Placebo, a label surrounded the syringes to maintain the blind. The syringes were transported from the pharmacy to the vaccination room in opaque containers to keep the study treatment blinded from the site staff and the study participants. The dedicated unblinded dosing team was assigned for the vaccine administration. The participant receiving the placebo was asked to look away from the injection site to keep the blind

Arms

Are arms mutually exclusive?	Yes
Arm title	MVA-NP+M1

Arm description:

MVA-NP+M1 & H3N2 Challenge

Arm type	Experimental
Investigational medicinal product name	MVA-NP+M1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Single dose of MVA-NP+M1 at 1.5 x 10E8 plaque forming unit, 0,5 mL given intramuscularly in the deltoid.

Arm title	Placebo

Arm description:

Placebo & H3N2 Challenge

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Saline Placebo 0,5 mL given intramuscularly in the deltoid.

Number of subjects in period 1	MVA-NP+M1	Placebo
Started	87	58
Completed	71	46
Not completed	16	12
Physician decision	4	2
Consent withdrawn by subject	1	2
Adverse event, non-fatal	-	1
Other	9	7
Pregnancy	1	-
Lost to follow-up	1	-

Baseline characteristics

Reporting groups	
Reporting group title	MVA-NP+M1
Reporting group description: MVA-NP+M1 & H3N2 Challenge	
Reporting group title	Placebo
Reporting group description: Placebo & H3N2 Challenge	

Reporting group values	MVA-NP+M1	Placebo	Total
Number of subjects	87	58	145
Age categorical Units: Subjects			
Adults (18-55 years)	87	58	145
Age continuous Units: years			
median	43.00	41.25	
full range (min-max)	18.5 to 55.9	19.9 to 55.7	-
Gender categorical Units: Subjects			
Female	47	31	78
Male	40	27	67
Race Units: Subjects			
Asian	2	0	2
Black or African American	4	0	4
Middle Eastern	0	1	1
White	81	57	138
Smoking status Units: Subjects			
Ex-smoker	27	18	45
Non-smoker	60	40	100
Height Units: cm			
median	172.40	172.30	
full range (min-max)	153.2 to 193.3	151.8 to 191.7	-
Weight Units: kg			
median	72.90	75.15	
full range (min-max)	53.2 to 118.8	54.6 to 105.6	-
BMI Units: kg/m2			
median	24.70	25.50	
full range (min-max)	19.0 to 32.0	19.2 to 31.2	-

End points

End points reporting groups

Reporting group title	MVA-NP+M1
Reporting group description: MVA-NP+M1 & H3N2 Challenge	
Reporting group title	Placebo
Reporting group description: Placebo & H3N2 Challenge	
Subject analysis set title	MVA-NP+M1 (ITT)
Subject analysis set type	Intention-to-treat
Subject analysis set description: Efficacy	
Subject analysis set title	Placebo (ITT)
Subject analysis set type	Intention-to-treat
Subject analysis set description: Efficacy	
Subject analysis set title	MVA-NP+M1 (PP)
Subject analysis set type	Per protocol
Subject analysis set description: Efficacy	
Subject analysis set title	Placebo (PP)
Subject analysis set type	Per protocol
Subject analysis set description: Efficacy	
Subject analysis set title	MVA-NP+M1 (Challenge)
Subject analysis set type	Safety analysis
Subject analysis set description: Safety	
Subject analysis set title	Placebo (Challenge)
Subject analysis set type	Safety analysis
Subject analysis set description: Safety	

Primary: Efficacy: Viral shedding AUC (qRT-PCR)

End point title	Efficacy: Viral shedding AUC (qRT-PCR)
End point description:	
End point type	Primary
End point timeframe: 9 days	

End point values	MVA-NP+M1 (ITT)	Placebo (ITT)	MVA-NP+M1 (PP)	Placebo (PP)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	71	47	70	47
Units: subjects				
least squares mean (confidence interval 95%)	649.7 (552.7 to 746.7)	726.1 (604.0 to 848.2)	646.5 (548.3 to 744.7)	726.1 (604.0 to 848.2)

End point values	MVA-NP+M1 (Challenge)	Placebo (Challenge)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71	47		
Units: subjects				
least squares mean (confidence interval 95%)	649.7 (552.7 to 746.7)	726.1 (604.0 to 848.2)		

Statistical analyses

Statistical analysis title	Viral Shedding AUC (qRT-PCR)
Comparison groups	MVA-NP+M1 (ITT) v Placebo (ITT)
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1711
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Viral Shedding AUC (qRT-PCR)
Comparison groups	MVA-NP+M1 (PP) v Placebo (PP)
Number of subjects included in analysis	117
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1654
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Viral Shedding AUC (qRT-PCR)
Comparison groups	MVA-NP+M1 (Challenge) v Placebo (Challenge)
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.1711
Method	Wilcoxon (Mann-Whitney)

Secondary: Efficacy: qPCR Attack Rate (qRT-PCR)

End point title	Efficacy: qPCR Attack Rate (qRT-PCR)

End point description:

End point type	Secondary

End point timeframe:

9 days

End point values	MVA-NP+M1 (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71	47		
Units: Percentage				
number (confidence interval 95%)				
qPCR-confirmed influenza	90.1 (80.7 to 95.9)	97.9 (88.7 to 99.9)		
No qPCR-confirmed influenza	9.9 (4.1 to 19.3)	2.1 (0.1 to 11.3)		

Statistical analyses

Statistical analysis title	qPCR Attack Rate
Comparison groups	MVA-NP+M1 (ITT) v Placebo (ITT)
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.143
Method	Fisher exact

Secondary: Efficacy: Culture Attack Rate (qCulture)

End point title	Efficacy: Culture Attack Rate (qCulture)

End point description:

End point type	Secondary

End point timeframe:

9 days

End point values	MVA-NP+M1 (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71	47		
Units: Percentage				
number (confidence interval 95%)				
Culture-confirmed influenza	77.5 (66.0 to 86.5)	85.1 (71.7 to 93.8)		
No Culure-confirmed	22.5 (13.5 to 34.0)	14.9 (6.2 to 28.3)		

Statistical analyses

Statistical analysis title	Culture Attack Rate
Comparison groups	MVA-NP+M1 (ITT) v Placebo (ITT)
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.3504
Method	Fisher exact

Secondary: Efficacy: Time to Start of Viral Shedding (qPCR)

End point title	Efficacy: Time to Start of Viral Shedding (qPCR)

End point description:

End point type	Secondary

End point timeframe:

11 days

End point values	MVA-NP+M1 (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71[1]	47[2]		
Units: Percentage				
median (confidence interval 95%)	24.40 (24.30 to 24.50)	24.30 (24.20 to 24.50)		

Notes:

[1] - subjects assessed = 71
subjects with event = 64
subjects censored = 7
[2] - subjects assessed = 47
subjects with event = 46
subjects censored = 1

Statistical analyses

Statistical analysis title	Time to Start of Viral Shedding
Comparison groups	MVA-NP+M1 (ITT) v Placebo (ITT)
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5558
Method	Logrank

Secondary: Efficacy: Time to Start of Viral Shedding (qCulture)

End point title	Efficacy: Time to Start of Viral Shedding (qCulture)

End point description:

End point type	Secondary

End point timeframe:

9 days

End point values	MVA-NP+M1 (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71[3]	47[4]		
Units: Subjects				
median (confidence interval 95%)	35.90 (35.60 to 48.00)	47.60 (24.70 to 48.50)		

Notes:

[3] - Subjects assessed = 71
Subjects with event = 55
Subjects censored = 16
[4] - Subjects assessed = 47
Subjects with event = 40
Subjects censored = 7

Statistical analyses

Statistical analysis title	Time to Start Viral Shedding (qCulture)
Comparison groups	MVA-NP+M1 (ITT) v Placebo (ITT)
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6534
Method	Logrank

Secondary: Efficacy: Peak Viral Shedding (qPCR)

End point title	Efficacy: Peak Viral Shedding (qPCR)

End point description:

End point type	Secondary

End point timeframe:

9 days

End point values	MVA-NP+M1 (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	64	46		
Units: Subjects				
arithmetic mean (confidence interval 95%)	5.876 (5.430 to 6.322)	6.054 (5.521 to 6.587)		

Statistical analyses

Statistical analysis title	Peak Viral Shedding
Comparison groups	MVA-NP+M1 (ITT) v Placebo (ITT)
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5485
Method	Wilcoxon (Mann-Whitney)

Secondary: Efficacy: Peak Viral Shedding (qCulture)

End point title	Efficacy: Peak Viral Shedding (qCulture)

End point description:

End point type	Secondary

End point timeframe:

9 days

End point values	MVA-NP+M1 (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	55	40		
Units: Subjects				
arithmetic mean (confidence interval 95%)	4.073 (3.683 to 4.463)	4.069 (3.442 to 4.695)		

Statistical analyses

Statistical analysis title	Peak Viral Shedding
Comparison groups	MVA-NP+M1 (ITT) v Placebo (ITT)
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6753
Method	Wilcoxon (Mann-Whitney)

Secondary: Efficacy: Time to Peak Viral Shedding (qPCR)

End point title	Efficacy: Time to Peak Viral Shedding (qPCR)

End point description:

End point type	Secondary

End point timeframe:

9 days

End point values	MVA-NP+M1 (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71[5]	47[6]		
Units: Subjects				
median (confidence interval 95%)	72.20 (60.00 to 96.00)	107.90 (72.20 to 119.80)		

Notes:

[5] - Subjects assessed = 71
Subjects with event = 64
Subjects censored = 7

[6] - Subjects assessed = 47
Subjects with event = 46
Subjects censored = 1

Statistical analyses

Statistical analysis title	Time to Peak of Viral Shedding
Comparison groups	Placebo (ITT) v MVA-NP+M1 (ITT)
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.711
Method	Logrank

Secondary: Efficacy: Time to Peak Viral Shedding (qCulture)

End point title	Efficacy: Time to Peak Viral Shedding (qCulture)

End point description:

End point type	Secondary

End point timeframe:
9 days

End point values	MVA-NP+M1 (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71[7]	47[8]		
Units: Subjects				
median (confidence interval 95%)	83.40 (60.10 to 96.30)	83.80 (60.10 to 96.40)		

Notes:

[7] - Subjects assessed = 71
Subjects with event = 55
Subjects censored = 16
[8] - Subjects assessed = 47
Subjects with event = 40
Subjects censored = 7

Statistical analyses

Statistical analysis title	Time to Peak of Viral Shedding (qCulture)
Comparison groups	MVA-NP+M1 (ITT) v Placebo (ITT)
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.4689
Method	Logrank

Secondary: Efficacy: Duration of Viral Shedding (qPCR)

End point title	Efficacy: Duration of Viral Shedding (qPCR)

End point description:

End point type	Secondary

End point timeframe:

11 days

End point values	MVA-NP+M1 (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	64	46		
Units: Days				
arithmetic mean (confidence interval 95%)	170.80 (157.08 to 184.52)	172.47 (156.99 to 187.94)		

Statistical analyses

No statistical analyses for this end point

Secondary: Efficacy: Duration of Viral Shedding (qCulture)

End point title	Efficacy: Duration of Viral Shedding (qCulture)

End point description:

End point type	Secondary

End point timeframe:

11 days

End point values	MVA-NP+M1 (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	55	40		
Units: Days				
arithmetic mean (confidence interval 95%)	118.19 (105.07 to 131.31)	121.78 (106.33 to 137.23)		

Statistical analyses

No statistical analyses for this end point

Secondary: Efficacy: AUC Composite Symptom Score

End point title	Efficacy: AUC Composite Symptom Score

End point description:

End point type	Secondary

End point timeframe:

11 days

End point values	MVA-NP+M1 (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71	47		
Units: Composite Symptom Score				
geometric mean (confidence interval 95%)	16.709 (11.568 to 21.850)	20.432 (13.753 to 27.112)		

Statistical analyses

Statistical analysis title	AUC of the Composite Symptom Score
Comparison groups	MVA-NP+M1 (ITT) v Placebo (ITT)
Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5001
Method	Wilcoxon (Mann-Whitney)

Secondary: Efficacy: Total Number of Days of Fever

End point title	Efficacy: Total Number of Days of Fever
End point description:	
End point type	Secondary
End point timeframe: 11 days	

End point values	MVA-NP+M1 (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71	47		
Units: Days				
arithmetic mean (confidence interval 95%)	0.0 (0.0 to 0.1)	0.0 (0.0 to 0.1)		

Statistical analyses

Statistical analysis title	Total Number of Days of Fever
Comparison groups	MVA-NP+M1 (ITT) v Placebo (ITT)

Number of subjects included in analysis	118
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.6799
Method	zero-inflated poisson model

Secondary: Efficacy: Total Mucus Production

End point title	Efficacy: Total Mucus Production

End point description:

End point type	Secondary

End point timeframe:

11 days

End point values	MVA-NP+M1 (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	26	18		
Units: Total Mucus Production				
arithmetic mean (confidence interval 95%)	31.09 (16.33 to 45.85)	38.21 (16.78 to 59.63)		

Statistical analyses

Statistical analysis title	Total Mucus Production
Comparison groups	MVA-NP+M1 (ITT) v Placebo (ITT)
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.5911
Method	Wilcoxon (Mann-Whitney)

Secondary: PD: Correlation Plots of T-Cell Responses (Elispot Results) to The Primary Endpoint, Symptom Scores and Influenza Incidence

End point title	PD: Correlation Plots of T-Cell Responses (Elispot Results) to The Primary Endpoint, Symptom Scores and Influenza Incidence

End point description:

End point type	Secondary

End point timeframe:

3 months

End point values	MVA-NP+M1 (ITT)	Placebo (ITT)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71	47[9]		
Units: Subjects	71	47		

Notes:

[9] - Challenge Day 28 = 46 subjects

Attachments (see zip file)	Correlation Plots of T Cell reponses/Table 14.2.4.1 Correlation

Statistical analyses

No statistical analyses for this end point

Secondary: Summary TEAE and Solicited Symptoms (Vaccination Phase)

End point title	Summary TEAE and Solicited Symptoms (Vaccination Phase)

End point description:

End point type	Secondary

End point timeframe:

7 days

End point values	MVA-NP+M1	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	87	58		
Units: Subjects				
TEAE	36	18		
Solicited symptom	84	24		
TEAE or solicited symptom	85	34		
Local solicited symptom	80	8		
Local Grade 3 solicited symptom	2	0		
Systemic solicited symptom	72	20		
Systemic Grade 3 solicited symptom	2	0		
TEAE of special interest	0	0		
Serious TEAE	1	0		
Non-serious TEAE	36	18		
Grade ≥ 3 TEAE	1	0		
Grade ≥ 3 TE laboratory toxicity	2	0		
Fatal TEAE	0	0		
TEAE related to treatment	10	4		
Serious TEAE related to treatment	1	0		
Grade ≥ 3 TEAE related to treatment	1	0		
TEAE for which study was discontinued	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Summary TEAE and Solicited Symptoms (Challenge Phase)

End point title	Summary TEAE and Solicited Symptoms (Challenge Phase)

End point description:

End point type	Secondary

End point timeframe:

17 days

End point values	MVA-NP+M1 (Challenge)	Placebo (Challenge)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	71	47		
Units: Subjects				
TEAE	30	21		
Solicited symptom	62	40		
TEAE or solicited symptom	65	42		
Local solicited symptom	59	39		
Local Grade 3 solicited symptom	0	0		
Systemic solicited symptom	45	32		
Sytemic Grade 3 solicited symptom	0	0		
TEAE of special interest	0	0		
Serious TEAE	0	1		
Non-serious TEAE	30	20		
Grade ≥3 TEAE	0	2		
Grade ≥3 TE laboratory toxicity	7	2		
Fatal TEAE	0	0		
TEAE related to challenge	7	5		
Serious TEAE related to challenge	0	0		
Grade ≥3 TEAE related to challenge	0	0		
TEAE for which study was discontinued	0	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent adverse events (TEAE) are defined as AEs starting during or after first administration of any study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	MVA-NP+M1 (Vaccination Phase)
Reporting group description: -	
Reporting group title	Placebo (Vaccination Phase)
Reporting group description: -	
Reporting group title	MVA-NP+M1 (Challenge Phase)
Reporting group description: -	
Reporting group title	Placebo (Challenge Phase)
Reporting group description: -	

Serious adverse events	MVA-NP+M1 (Vaccination Phase)	Placebo (Vaccination Phase)	MVA-NP+M1 (Challenge Phase)
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 87 (1.15%)	0 / 58 (0.00%)	0 / 71 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Pregnancy, puerperium and perinatal conditions			
Foetal death			
subjects affected / exposed	1 / 87 (1.15%)	0 / 58 (0.00%)	0 / 71 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Psychiatric disorders			
Acute psychosis			
subjects affected / exposed	0 / 87 (0.00%)	0 / 58 (0.00%)	0 / 71 (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	Placebo (Challenge Phase)		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 47 (2.13%)		
number of deaths (all causes)	0		

number of deaths resulting from adverse events	0		
Pregnancy, puerperium and perinatal conditions			
Foetal death			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Acute psychosis			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	MVA-NP+M1 (Vaccination Phase)	Placebo (Vaccination Phase)	MVA-NP+M1 (Challenge Phase)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	36 / 87 (41.38%)	18 / 58 (31.03%)	30 / 71 (42.25%)
Surgical and medical procedures			
Scar excision			
subjects affected / exposed	1 / 87 (1.15%)	0 / 58 (0.00%)	0 / 71 (0.00%)
occurrences (all)	1	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 87 (0.00%)	0 / 58 (0.00%)	1 / 71 (1.41%)
occurrences (all)	0	0	1
Inflammation			
subjects affected / exposed	1 / 87 (1.15%)	0 / 58 (0.00%)	0 / 71 (0.00%)
occurrences (all)	1	0	0
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	1 / 87 (1.15%)	0 / 58 (0.00%)	2 / 71 (2.82%)
occurrences (all)	1	0	2
Respiratory, thoracic and mediastinal disorders			

Throat irritation			
subjects affected / exposed	3 / 87 (3.45%)	2 / 58 (3.45%)	0 / 71 (0.00%)
occurrences (all)	3	2	0
Epistaxis			
subjects affected / exposed	3 / 87 (3.45%)	0 / 58 (0.00%)	2 / 71 (2.82%)
occurrences (all)	3	0	2
Rhinorrhoea			
subjects affected / exposed	2 / 87 (2.30%)	1 / 58 (1.72%)	0 / 71 (0.00%)
occurrences (all)	2	1	0
Sneezing			
subjects affected / exposed	1 / 87 (1.15%)	1 / 58 (1.72%)	0 / 71 (0.00%)
occurrences (all)	1	1	0
Dysphonia			
subjects affected / exposed	0 / 87 (0.00%)	0 / 58 (0.00%)	0 / 71 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Subcutaneous haematoma			
subjects affected / exposed	1 / 87 (1.15%)	1 / 58 (1.72%)	0 / 71 (0.00%)
occurrences (all)	1	1	0
Joint injury			
subjects affected / exposed	0 / 87 (0.00%)	0 / 58 (0.00%)	1 / 71 (1.41%)
occurrences (all)	0	0	1
Skin wound			
subjects affected / exposed	0 / 87 (0.00%)	0 / 58 (0.00%)	0 / 71 (0.00%)
occurrences (all)	0	0	0
Arthropod bite			
subjects affected / exposed	0 / 87 (0.00%)	1 / 58 (1.72%)	0 / 71 (0.00%)
occurrences (all)	0	1	0
Ligament sprain			
subjects affected / exposed	1 / 87 (1.15%)	0 / 58 (0.00%)	0 / 71 (0.00%)
occurrences (all)	1	0	0
Limb injury			
subjects affected / exposed	0 / 87 (0.00%)	1 / 58 (1.72%)	0 / 71 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			

Atrial flutter			
subjects affected / exposed	0 / 87 (0.00%)	0 / 58 (0.00%)	0 / 71 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	5 / 87 (5.75%)	2 / 58 (3.45%)	2 / 71 (2.82%)
occurrences (all)	5	2	2
Presyncope			
subjects affected / exposed	0 / 87 (0.00%)	0 / 58 (0.00%)	1 / 71 (1.41%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Ear discomfort			
subjects affected / exposed	0 / 87 (0.00%)	1 / 58 (1.72%)	2 / 71 (2.82%)
occurrences (all)	0	1	2
Eye disorders			
Eye irritation			
subjects affected / exposed	0 / 87 (0.00%)	0 / 58 (0.00%)	2 / 71 (2.82%)
occurrences (all)	0	0	2
Conjunctival hyperaemia			
subjects affected / exposed	0 / 87 (0.00%)	0 / 58 (0.00%)	0 / 71 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased			
subjects affected / exposed	2 / 87 (2.30%)	0 / 58 (0.00%)	0 / 71 (0.00%)
occurrences (all)	2	0	0
Swelling of eyelid			
subjects affected / exposed	1 / 87 (1.15%)	0 / 58 (0.00%)	0 / 71 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	5 / 87 (5.75%)	3 / 58 (5.17%)	3 / 71 (4.23%)
occurrences (all)	5	3	3
Nausea			
subjects affected / exposed	0 / 87 (0.00%)	0 / 58 (0.00%)	1 / 71 (1.41%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	0 / 87 (0.00%)	0 / 58 (0.00%)	0 / 71 (0.00%)
occurrences (all)	0	0	0

Constipation			
subjects affected / exposed	0 / 87 (0.00%)	0 / 58 (0.00%)	1 / 71 (1.41%)
occurrences (all)	0	0	1
Dry mouth			
subjects affected / exposed	0 / 87 (0.00%)	0 / 58 (0.00%)	0 / 71 (0.00%)
occurrences (all)	0	0	0
Regurgitation			
subjects affected / exposed	0 / 87 (0.00%)	0 / 58 (0.00%)	1 / 71 (1.41%)
occurrences (all)	0	0	1
Toothache			
subjects affected / exposed	0 / 87 (0.00%)	0 / 58 (0.00%)	1 / 71 (1.41%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	0 / 87 (0.00%)	0 / 58 (0.00%)	1 / 71 (1.41%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	3 / 87 (3.45%)	1 / 58 (1.72%)	2 / 71 (2.82%)
occurrences (all)	3	1	2
Skin irritation			
subjects affected / exposed	2 / 87 (2.30%)	1 / 58 (1.72%)	3 / 71 (4.23%)
occurrences (all)	2	1	3
Dry skin			
subjects affected / exposed	0 / 87 (0.00%)	0 / 58 (0.00%)	1 / 71 (1.41%)
occurrences (all)	0	0	1
Eczema			
subjects affected / exposed	1 / 87 (1.15%)	0 / 58 (0.00%)	0 / 71 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	3 / 87 (3.45%)	0 / 58 (0.00%)	4 / 71 (5.63%)
occurrences (all)	4	0	4
Neck pain			
subjects affected / exposed	2 / 87 (2.30%)	1 / 58 (1.72%)	0 / 71 (0.00%)
occurrences (all)	2	1	0
Bursitis			

subjects affected / exposed	0 / 87 (0.00%)	0 / 58 (0.00%)	1 / 71 (1.41%)
occurrences (all)	0	0	1
Flank pain			
subjects affected / exposed	0 / 87 (0.00%)	0 / 58 (0.00%)	0 / 71 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 87 (0.00%)	0 / 58 (0.00%)	1 / 71 (1.41%)
occurrences (all)	0	0	1
Musculoskeletal stiffness			
subjects affected / exposed	0 / 87 (0.00%)	0 / 58 (0.00%)	1 / 71 (1.41%)
occurrences (all)	0	0	1
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	6 / 87 (6.90%)	4 / 58 (6.90%)	0 / 71 (0.00%)
occurrences (all)	7	4	0
Gastroenteritis			
subjects affected / exposed	0 / 87 (0.00%)	2 / 58 (3.45%)	0 / 71 (0.00%)
occurrences (all)	0	2	0
Oral herpes			
subjects affected / exposed	2 / 87 (2.30%)	0 / 58 (0.00%)	1 / 71 (1.41%)
occurrences (all)	2	0	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 87 (0.00%)	0 / 58 (0.00%)	0 / 71 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 87 (1.15%)	0 / 58 (0.00%)	0 / 71 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Placebo (Challenge Phase)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 47 (44.68%)		
Surgical and medical procedures			
Scar excision			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences (all)	0		
General disorders and administration			

site conditions			
Asthenia			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences (all)	0		
Inflammation			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Dysmenorrhoea			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Throat irritation			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences (all)	0		
Epistaxis			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences (all)	0		
Rhinorrhoea			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences (all)	0		
Sneezing			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences (all)	0		
Dysphonia			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Subcutaneous haematoma			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences (all)	0		
Joint injury			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences (all)	0		
Skin wound			

subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Arthropod bite subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0		
Ligament sprain subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0		
Limb injury subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0		
Cardiac disorders Atrial flutter subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Presyncope subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0		
Ear and labyrinth disorders Ear discomfort subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0		
Eye disorders Eye irritation subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0		
Conjunctival hyperaemia subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Lacrimation increased subjects affected / exposed occurrences (all)	0 / 47 (0.00%) 0		
Swelling of eyelid			

subjects affected / exposed	0 / 47 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Abdominal pain			
subjects affected / exposed	2 / 47 (4.26%)		
occurrences (all)	2		
Constipation			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences (all)	0		
Dry mouth			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Regurgitation			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences (all)	0		
Toothache			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences (all)	0		
Skin irritation			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Dry skin			

subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Eczema			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	6 / 47 (12.77%)		
occurrences (all)	6		
Neck pain			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Bursitis			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences (all)	0		
Flank pain			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Musculoskeletal pain			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences (all)	0		
Musculoskeletal stiffness			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences (all)	0		
Gastroenteritis			
subjects affected / exposed	0 / 47 (0.00%)		
occurrences (all)	0		
Oral herpes			
subjects affected / exposed	1 / 47 (2.13%)		
occurrences (all)	1		
Upper respiratory tract infection			

subjects affected / exposed occurrences (all)	1 / 47 (2.13%) 1		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	 0 / 47 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 April 2019	- Additional timepoints in challenge period to measure transcriptomics. Sodium and potassium tests were added to the biochemistry test in the challenge period. - The exclusion criteria were split in two categories i.e., study entry and challenge period entry. - The process that maintains the double blind throughout the study was amended to provide a robust procedure.
17 July 2019	- MNT increased from ≤10 to <20. - Attack rate change from 90% to 83%. - A clarification added the challenge risk section.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported