

**Clinical trial results:****A Phase I Randomized, Double-Blind Trial of the Safety and Immunogenicity of FluMist® A Live, Intranasal Influenza Virus Vaccine vs. Placebo in Immunocompromised Children Ages 5 Through 17 Years of Age****Summary**

EudraCT number	2017-000849-50
Trial protocol	Outside EU/EEA
Global end of trial date	31 March 2008

Results information

Result version number	v1 (current)
This version publication date	03 January 2018
First version publication date	03 January 2018

Trial information**Trial identification**

Sponsor protocol code	MI-CP114
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00112112
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	MedImmune, LLC
Sponsor organisation address	One MedImmune Way, Gaithersburg, MD, United States, 20837
Public contact	Raburn Mallory, MedImmune, LLC, +1 3013980000, malloryr@medimmune.com
Scientific contact	Raburn Mallory, MedImmune, LLC, +1 3013980000, malloryr@medimmune.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	31 March 2008
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	31 March 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study was to describe the safety of FluMist compared with placebo in mild to moderately immunocompromised children with cancer.

Protection of trial subjects:

The conduct of this clinical study met all local and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and are consistent with International Conference on Harmonization guideline: Good Clinical Practice, and applicable regulatory requirements. Participants signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 August 2005
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	United States: 20
Worldwide total number of subjects	20
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	8
Adolescents (12-17 years)	12
Adults (18-64 years)	0
From 65 to 84 years	0

Subject disposition

Recruitment

Recruitment details:

A total of 20 participants, 10 in the FluMist group and 10 in the placebo group, were enrolled in the study across 4 sites in the United States of America.

Pre-assignment

Screening details:

A total of 20 participants were randomized in a 1:1 ratio to either the FluMist or placebo group. Four participants were enrolled and treated in 2005, 8 in 2006, and 8 in 2007; each subset was assessed for vaccine-related serious adverse events prior to enrollment of the next subset.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Placebo intranasal mist was composed of allantoic fluid stabilized with buffer containing sucrose, potassium phosphate, and monosodium glutamate. The total volume of 0.5 milliliter (mL) was administered intranasally with a spray applicator (approximately 0.25 mL into each nostril).

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray
Routes of administration	Nasal use

Dosage and administration details:

The total volume of 0.5 mL of placebo was administered intranasally with a spray applicator (approximately 0.25 mL into each nostril).

Arm title	FluMist
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Arm description:

The total volume of 0.5 mL was administered intranasally with a spray applicator (approximately 0.25 mL into each nostril). Each dose contained approximately 10^7 median tissue culture infectious dose (TCID₅₀) of each of three influenza virus strains.

Arm type	Experimental
Investigational medicinal product name	FluMist
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray
Routes of administration	Nasal use

Dosage and administration details:

The total volume of 0.5 mL of FluMist was administered intranasally with a spray applicator (approximately 0.25 mL into each nostril).

Number of subjects in period 1	Placebo	FluMist
Started	10	10
Completed	10	10

Baseline characteristics

Reporting groups

Reporting group title	Placebo
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Reporting group description:

Placebo intranasal mist was composed of allantoic fluid stabilized with buffer containing sucrose, potassium phosphate, and monosodium glutamate. The total volume of 0.5 milliliter (mL) was administered intranasally with a spray applicator (approximately 0.25 mL into each nostril).

Reporting group title	FluMist
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Reporting group description:

The total volume of 0.5 mL was administered intranasally with a spray applicator (approximately 0.25 mL into each nostril). Each dose contained approximately 10^7 median tissue culture infectious dose (TCID₅₀) of each of three influenza virus strains.

Reporting group values	Placebo	FluMist	Total
Number of subjects	10	10	20
Age categorical Units: Subjects			
Children (2-11 years)	4	4	8
Adolescents (12-17 years)	6	6	12
Age Continuous Units: Years			
arithmetic mean	12.2	12.2	
standard deviation	± 3.8	± 3.9	-
Gender, Male/Female Units: Subjects			
Male	6	3	9
Female	4	7	11

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Placebo intranasal mist was composed of allantoin fluid stabilized with buffer containing sucrose, potassium phosphate, and monosodium glutamate. The total volume of 0.5 milliliter (mL) was administered intranasally with a spray applicator (approximately 0.25 mL into each nostril).	
Reporting group title	FluMist
Reporting group description: The total volume of 0.5 mL was administered intranasally with a spray applicator (approximately 0.25 mL into each nostril). Each dose contained approximately 10^7 median tissue culture infectious dose (TCID ₅₀) of each of three influenza virus strains.	

Primary: Number of Participants who had Reactogenicity Events (REs)

End point title	Number of Participants who had Reactogenicity Events (REs) ^[1]
End point description: Reactogenicity events (REs) are predefined solicited adverse events (AEs) that can potentially occur after vaccine administration. The REs For this study included fever, runny nose/nasal congestion, sore throat, cough, vomiting, headache, muscle aches, chills, tiredness, and irritability. Participants who received any study vaccine and had any follow-up for REs and/or AEs were analysed for this end point. One participant in FluMist group did not have any RE data and was excluded from the RE analysis.	
End point type	Primary
End point timeframe: 0-42 days after study vaccination	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Statistical analysis was not applicable since there were no inferential statistics planned for primary outcome measures, only descriptive statistics were reported.

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Participants	9	8		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants who had Serious Adverse Events (SAEs)

End point title	Number of Participants who had Serious Adverse Events
End point description: An SAE is any AE that results in any of the following outcomes: •Death • Life-threatening • Inpatient hospitalization or prolongation of existing hospitalization • Persistent or significant disability or incapacity • Congenital anomaly/birth defect (in the offspring of a study participant) • An important medical event that may may jeopardize the study participant and may require medical or surgical intervention to prevent one of the outcomes listed above. Participants who received any study vaccine and had any follow-up for REs and/or AEs were analysed for this end point.	

End point type	Primary
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End point timeframe:

0-180 days after study vaccination

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Statistical analysis was not applicable since there were no inferential statistics planned for primary outcome measures, only descriptive statistics were reported.

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: Participants	3	1		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants who had Adverse Events (AEs)

End point title	Number of Participants who had Adverse Events (AEs) ^[3]
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End point description:

An AE is any untoward medical occurrence in a patient or clinical investigations study participant administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Participants who received any study vaccine and had any follow-up for REs and/or AEs were analysed for this end point.

End point type	Primary
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End point timeframe:

0-42 days after study vaccination

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Statistical analysis was not applicable since there were no inferential statistics planned for primary outcome measures, only descriptive statistics were reported.

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: Participants	10	6		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Significant new Medical Conditions (SNMCs)

End point title	Number of Significant new Medical Conditions (SNMCs) ^[4]
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End point description:

A significant new medical condition is defined as a new diagnosis of a chronic medical condition that

does not meet the criteria of a SAE. Participants who received any study vaccine and had any follow-up for REs and/or AEs were analysed for this end point.

End point type	Primary
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End point timeframe:

43-180 days after study vaccination

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Statistical analysis was not applicable since there were no inferential statistics planned for primary outcome measures, only descriptive statistics were reported.

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: Events	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Shedding Vaccine-like Virus

End point title	Number of Participants Shedding Vaccine-like Virus
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End point description:

Number of participants with nasal swab samples that contained vaccine-like virus are reported. Participants who received any study vaccine and had any follow-up for REs and/or AEs were analysed for this end point.

End point type	Secondary
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End point timeframe:

3-5 days after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: Participants	0	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Shedding Vaccine-like Virus

End point title	Number of Participants Shedding Vaccine-like Virus
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End point description:

Number of participants with nasal swab samples that contained vaccine-like virus are reported. Participants who received any study vaccine and had any follow-up for REs and/or AEs were analysed for this end point.

End point type	Secondary
End point timeframe:	
7-10 days after study vaccination	

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: Participants	0	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Shedding Vaccine-like Virus

End point title	Number of Participants Shedding Vaccine-like Virus
End point description:	
Number of participants with nasal swab samples that contained vaccine-like virus are reported. Participants who received any study vaccine and had any follow-up for REs and/or AEs were analysed for this end point.	
End point type	Secondary
End point timeframe:	
14-28 days after study vaccination	

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Shedding Vaccine-like Virus

End point title	Number of Participants Shedding Vaccine-like Virus
End point description:	
Number of participants with nasal swab samples that contained vaccine-like virus are reported. Sample was collected at this time point only if health assessment indicated presence of a respiratory illness, including otitis media. Participants who received any study vaccine and had any follow-up for REs and/or AEs were analysed for this end point.	
End point type	Secondary
End point timeframe:	
35-42 days after study vaccination	

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Shedding Vaccine-like Virus

End point title	Number of Participants Shedding Vaccine-like Virus
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End point description:

Number of participants with nasal swab samples that contained vaccine-like virus are reported. Participants who received any study vaccine and had any follow-up for REs and/or AEs were analysed for this end point.

End point type	Secondary
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End point timeframe:

Unscheduled visits occurring during 0-42 days after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	10		
Units: Participants	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: T- and B-lymphocyte Subsets by Flow Cytometry - Cluster of Differentiation (CD) 19

End point title	T- and B-lymphocyte Subsets by Flow Cytometry - Cluster of Differentiation (CD) 19
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End point description:

Mean and standard deviation results of CD19 lymphocyte subsets as a percentage of total lymphocytes. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type	Secondary
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End point timeframe:

pre-dosing (Day 0)

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Percentage of lymphocytes				
arithmetic mean (standard deviation)	4.8 (± 8.3)	8.6 (± 7.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: T- and B-lymphocyte Subsets by Flow Cytometry - CD3

End point title	T- and B-lymphocyte Subsets by Flow Cytometry - CD3			
End point description:	Mean and standard deviation results of CD3 lymphocyte subsets as a percentage of total lymphocytes. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.			
End point type	Secondary			
End point timeframe:	pre-dosing (Day 0)			

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Percentage of lymphocytes				
arithmetic mean (standard deviation)	89.1 (± 10.3)	83.6 (± 8.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: T- and B-lymphocyte Subsets by Flow Cytometry - CD4

End point title	T- and B-lymphocyte Subsets by Flow Cytometry - CD4			
End point description:	Mean and standard deviation results of CD4 lymphocyte subsets as a percentage of total lymphocytes. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.			
End point type	Secondary			
End point timeframe:	pre-dosing (Day 0)			

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Percentage of lymphocytes				
arithmetic mean (standard deviation)	46.7 (± 7.5)	47.3 (± 9.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: T- and B-lymphocyte Subsets by Flow Cytometry - CD8

End point title	T- and B-lymphocyte Subsets by Flow Cytometry - CD8
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End point description:

Mean and standard deviation results of CD8 lymphocyte subsets as a percentage of total lymphocytes. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type	Secondary
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End point timeframe:

pre-dosing (Day 0)

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Percentage of lymphocytes				
arithmetic mean (standard deviation)	38.8 (± 7.8)	31.4 (± 8.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: T- and B-lymphocyte Subsets by Flow Cytometry - CD19

End point title	T- and B-lymphocyte Subsets by Flow Cytometry - CD19
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End point description:

Mean and standard deviation results of CD19 lymphocyte subsets as a percentage of total lymphocytes. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type	Secondary
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End point timeframe:

7-10 days after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	9		
Units: Percentage of lymphocytes				
arithmetic mean (standard deviation)	5.1 (\pm 8.6)	10.2 (\pm 10.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: T- and B-lymphocyte Subsets by Flow Cytometry - CD3

End point title	T- and B-lymphocyte Subsets by Flow Cytometry - CD3
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End point description:

Mean and standard deviation results of CD3 lymphocyte subsets as a percentage of total lymphocytes. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type	Secondary
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End point timeframe:

7-10 days after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	9		
Units: Percentage of lymphocytes				
arithmetic mean (standard deviation)	89.9 (\pm 11.6)	82.0 (\pm 9.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: T- and B-lymphocyte Subsets by Flow Cytometry - CD4

End point title	T- and B-lymphocyte Subsets by Flow Cytometry - CD4
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End point description:

Mean and standard deviation results of CD4 lymphocyte subsets as a percentage of total lymphocytes. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type	Secondary
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End point timeframe:

7-10 days after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	9		
Units: Percentage of lymphocytes				
arithmetic mean (standard deviation)	46.5 (± 11.4)	48.2 (± 11.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: T- and B-lymphocyte Subsets by Flow Cytometry - CD8

End point title	T- and B-lymphocyte Subsets by Flow Cytometry - CD8
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End point description:

Mean and standard deviation results of CD8 lymphocyte subsets as a percentage of total lymphocytes. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type	Secondary
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End point timeframe:

7-10 days after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	9		
Units: Percentage of lymphocytes				
arithmetic mean (standard deviation)	39.6 (± 10.1)	27.9 (± 8.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Interferon (INF)-Gamma

End point title	Interferon (INF)-Gamma
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End point description:

Mean and standard deviation for INF-Gamma (spots-forming cells per 10⁵ T cells) is reported. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type	Secondary
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End point timeframe:

pre-dosing (Day 0)

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	7		
Units: Cells per 10 ⁵ T cells				
arithmetic mean (standard deviation)	16.5 (± 25.9)	17.0 (± 27.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: INF-Gamma

End point title	INF-Gamma
End point description:	Mean and standard deviation for INF-Gamma (spots-forming cells per 10 ⁵ T cells) is reported. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.
End point type	Secondary
End point timeframe:	7-10 days after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	7		
Units: Cells per 10 ⁵ T cells				
arithmetic mean (standard deviation)	7.5 (± 7.6)	28.6 (± 43.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: INF-Gamma

End point title	INF-Gamma
End point description:	Mean and standard deviation for INF-Gamma (spots-forming cells per 10 ⁵ T cells) is reported. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.
End point type	Secondary
End point timeframe:	35-42 days after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	7		
Units: Cells per 10 ⁵ T cells				
arithmetic mean (standard deviation)	16.6 (± 27.0)	28.0 (± 38.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Interleukin (IL)-4

End point title	Interleukin (IL)-4
End point description:	Mean and standard deviation for IL-4 (spots-forming cells per 10 ⁵ T cells) is reported. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.
End point type	Secondary
End point timeframe:	pre-dosing (Day 0)

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	8		
Units: Cells per 10 ⁵ T cells				
arithmetic mean (standard deviation)	5.5 (± 8.4)	2.6 (± 4.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: IL-4

End point title	IL-4
End point description:	Mean and standard deviation for IL-4 (spots-forming cells per 10 ⁵ T cells) is reported. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.
End point type	Secondary
End point timeframe:	7-10 days after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	8		
Units: Cells per 10 ⁵ T cells				
arithmetic mean (standard deviation)	2.6 (± 3.5)	1.9 (± 2.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: IL-4

End point title	IL-4
End point description:	Mean and standard deviation for IL-4 (spots-forming cells per 10 ⁵ T cells) is reported. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.
End point type	Secondary
End point timeframe:	35-42 days after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	8		
Units: Cells per 10 ⁵ T cells				
arithmetic mean (standard deviation)	4.7 (± 6.1)	2.9 (± 3.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Human Leukocyte Antigen (HLA) Matched Tetramers CD8+

End point title	Human Leukocyte Antigen (HLA) Matched Tetramers CD8+
End point description:	The antigen-specific response of the T cell populations was measured using HLA-matched tetramers specific for human CD8 cell populations. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.
End point type	Secondary
End point timeframe:	pre-dosing (Day 0)

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	6		
Units: Percentage of lymphocytes				
arithmetic mean (standard deviation)	12.778 (\pm 6.579)	11.045 (\pm 6.452)		

Statistical analyses

No statistical analyses for this end point

Secondary: HLA Matched Tetramers CD8+

End point title	HLA Matched Tetramers CD8+
End point description:	The antigen-specific response of the T cell populations was measured using HLA-matched tetramers specific for human CD8 cell populations. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.
End point type	Secondary
End point timeframe:	7-10 days after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	6		
Units: Percentage of lymphocytes				
arithmetic mean (standard deviation)	8.632 (\pm 4.126)	8.048 (\pm 6.701)		

Statistical analyses

No statistical analyses for this end point

Secondary: HLA Matched Tetramers CD8+

End point title	HLA Matched Tetramers CD8+
End point description:	The antigen-specific response of the T cell populations was measured using HLA-matched tetramers specific for human CD8 cell populations. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.
End point type	Secondary

End point timeframe:
35-42 days after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	6		
Units: Percentage of lymphocytes				
arithmetic mean (standard deviation)	12.922 (\pm 8.607)	7.997 (\pm 3.143)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Experienced a \geq 4-fold Rise in Serum Influenza A/H1N1 Hemagglutination Inhibition (HAI) Titers From Baseline to Day 35-42

End point title	Number of Participants who Experienced a \geq 4-fold Rise in Serum Influenza A/H1N1 Hemagglutination Inhibition (HAI) Titers From Baseline to Day 35-42
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End point description:

Participants with a geometric mean fold-rise in influenza-specific nasal HAI titers \geq 4 from baseline are reported. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had samples available for the specified days were analysed for this end point.

End point type	Secondary
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End point timeframe:

Baseline (Pre-dosing on Day 0) and Day 35-42 after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Participants	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Experienced a \geq 4-fold Rise in Serum Influenza A/H3N2 HAI Titers From Baseline to Day 35-42

End point title	Number of Participants who Experienced a \geq 4-fold Rise in Serum Influenza A/H3N2 HAI Titers From Baseline to Day 35-42
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End point description:

Participants with a geometric mean fold-rise in influenza-specific nasal HAI titers ≥ 4 from baseline are reported. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had samples available for the specified days were analysed for this end point.

End point type Secondary

End point timeframe:

Baseline (Pre-dosing on Day 0) and Day 35-42 after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Participants	0	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Experienced a ≥ 4 -fold Rise in Serum Influenza B HAI Titers From Baseline to Day 35-42

End point title Number of Participants who Experienced a ≥ 4 -fold Rise in Serum Influenza B HAI Titers From Baseline to Day 35-42

End point description:

Participants with a geometric mean fold-rise in influenza-specific nasal HAI titers ≥ 4 from baseline are reported. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had samples available for the specified days were analysed for this end point.

End point type Secondary

End point timeframe:

Baseline (Pre-dosing on Day 0) and Day 35-42 after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Participants	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Experienced a ≥ 4 -fold Rise in Serum Influenza A/H1N1 Microneutralization Titers From Baseline to Day 35-42

End point title Number of Participants who Experienced a ≥ 4 -fold Rise in

End point description:

Participants with a geometric mean fold-rise in influenza-specific nasal microneutralization titers ≥ 4 from baseline are reported. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had samples available for the specified days were analysed for this end point.

End point type Secondary

End point timeframe:

Baseline (Pre-dosing on Day 0) and Day 35-42 after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Participants	0	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Experienced a ≥ 4 -fold Rise in Serum Influenza A/H3N2 Microneutralization Titers From Baseline to Day 35-42

End point title Number of Participants who Experienced a ≥ 4 -fold Rise in Serum Influenza A/H3N2 Microneutralization Titers From Baseline to Day 35-42

End point description:

Participants with a geometric mean fold-rise in influenza-specific nasal microneutralization titers ≥ 4 from baseline are reported. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had samples available for the specified days were analysed for this end point.

End point type Secondary

End point timeframe:

Baseline (Pre-dosing on Day 0) and Day 35-42 after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Participants	0	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants who Experienced a \geq 4-fold Rise in Serum Influenza B Microneutralization Titers From Baseline to Day 35-42

End point title	Number of Participants who Experienced a \geq 4-fold Rise in Serum Influenza B Microneutralization Titers From Baseline to Day 35-42
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End point description:

Participants with a geometric mean fold-rise in influenza-specific nasal microneutralization titers \geq 4 from baseline are reported. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had samples available for the specified days were analysed for this end point.

End point type	Secondary
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End point timeframe:

Baseline (Pre-dosing on Day 0) and Day 35-42 after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Participants	0	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Influenza A/H1N1 Immunoglobulin A (IgA)

End point title	Influenza A/H1N1 Immunoglobulin A (IgA)
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End point description:

Mean of influenza-specific IgA from nasal swab is reported. Titers of < 1 were assigned the value of 0.5. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type	Secondary
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End point timeframe:

pre-dosing (Day 0)

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Titer				
arithmetic mean (standard deviation)	0.5 (\pm 0.0)	0.8 (\pm 0.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Influenza A/H1N1 IgA

End point title Influenza A/H1N1 IgA

End point description:

Mean of influenza-specific IgA from nasal swab is reported. Titers of < 1 were assigned the value of 0.5. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type Secondary

End point timeframe:

3-5 days after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Titer				
arithmetic mean (standard deviation)	0.5 (\pm 0.0)	0.8 (\pm 0.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Influenza A/H1N1 IgA

End point title Influenza A/H1N1 IgA

End point description:

Mean of influenza-specific IgA from nasal swab is reported. Titers of < 1 were assigned the value of 0.5. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type Secondary

End point timeframe:

7-10 days after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Titer				
arithmetic mean (standard deviation)	0.5 (\pm 0.0)	1.1 (\pm 1.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Influenza A/H1N1 IgA

End point title Influenza A/H1N1 IgA

End point description:

Mean of influenza-specific IgA from nasal swab is reported. Titers of < 1 were assigned the value of 0.5. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type Secondary

End point timeframe:

14-28 days after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Titer				
arithmetic mean (standard deviation)	1.1 (± 1.3)	0.9 (± 0.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Influenza A/H1N1 IgA

End point title Influenza A/H1N1 IgA

End point description:

Mean of influenza-specific IgA from nasal swab is reported. Titers of < 1 were assigned the value of 0.5. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type Secondary

End point timeframe:

35-42 days after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Titer				
arithmetic mean (standard deviation)	0.5 (± 0.0)	1.3 (± 1.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Influenza A/H3N2 IgA

End point title Influenza A/H3N2 IgA

End point description:

Mean of influenza-specific IgA from nasal swab is reported. Titers of < 1 were assigned the value of 0.5. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type Secondary

End point timeframe:

pre-dosing (Day 0)

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Titer				
arithmetic mean (standard deviation)	0.7 (\pm 0.5)	1.0 (\pm 0.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Influenza A/H3N2 IgA

End point title Influenza A/H3N2 IgA

End point description:

Mean of influenza-specific IgA from nasal swab is reported. Titers of < 1 were assigned the value of 0.5. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type Secondary

End point timeframe:

3-5 days after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Titer				
arithmetic mean (standard deviation)	0.5 (\pm 0.0)	0.7 (\pm 0.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Influenza A/H3N2 IgA

End point title Influenza A/H3N2 IgA

End point description:

Mean of influenza-specific IgA from nasal swab is reported. Titers of < 1 were assigned the value of 0.5. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type Secondary

End point timeframe:

7-10 days after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Titer				
arithmetic mean (standard deviation)	0.7 (\pm 0.5)	1.2 (\pm 0.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Influenza A/H3N2 IgA

End point title Influenza A/H3N2 IgA

End point description:

Mean of influenza-specific IgA from nasal swab is reported. Titers of < 1 were assigned the value of 0.5. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type Secondary

End point timeframe:

14-28 days after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Titer				
arithmetic mean (standard deviation)	1.1 (\pm 0.9)	0.7 (\pm 0.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Influenza A/H3N2 IgA

End point title Influenza A/H3N2 IgA

End point description:

Mean of influenza-specific IgA from nasal swab is reported. Titers of < 1 were assigned the value of 0.5. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type Secondary

End point timeframe:

35-42 days after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Titer				
arithmetic mean (standard deviation)	0.5 (\pm 0.0)	1.7 (\pm 1.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Influenza B IgA

End point title Influenza B IgA

End point description:

Mean of influenza-specific IgA from nasal swab is reported. Titers of < 1 were assigned the value of 0.5. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type Secondary

End point timeframe:

pre-dosing (Day 0)

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Titer				
arithmetic mean (standard deviation)	0.5 (\pm 0.0)	0.5 (\pm 0.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Influenza B IgA

End point title Influenza B IgA

End point description:

Mean of influenza-specific IgA from nasal swab is reported. Titers of < 1 were assigned the value of 0.5. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type Secondary

End point timeframe:

3-5 days after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Titer				
arithmetic mean (standard deviation)	0.5 (± 0.0)	0.5 (± 0.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Influenza B IgA

End point title Influenza B IgA

End point description:

Mean of influenza-specific IgA from nasal swab is reported. Titers of < 1 were assigned the value of 0.5. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type Secondary

End point timeframe:

7-10 days after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Titer				
arithmetic mean (standard deviation)	0.5 (± 0.0)	0.5 (± 0.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Influenza B IgA

End point title Influenza B IgA

End point description:

Mean of influenza-specific IgA from nasal swab is reported. Titers of < 1 were assigned the value of 0.5. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type Secondary

End point timeframe:

14-28 days after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Titer				
arithmetic mean (standard deviation)	0.5 (\pm 0.0)	0.5 (\pm 0.0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Influenza B IgA

End point title Influenza B IgA

End point description:

Mean of influenza-specific IgA from nasal swab is reported. Titers of < 1 were assigned the value of 0.5. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type Secondary

End point timeframe:

35-42 days after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Titer				
arithmetic mean (standard deviation)	0.5 (\pm 0.0)	0.7 (\pm 0.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: T- and B-lymphocyte Subsets by Flow Cytometry - CD56

End point title T- and B-lymphocyte Subsets by Flow Cytometry - CD56

End point description:

Mean and standard deviation results of CD56 lymphocyte subsets is reported. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type Secondary

End point timeframe:

pre-dosing (Day 0)

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Percentage of lymphocytes				
arithmetic mean (standard deviation)	5.2 (\pm 3.2)	7.6 (\pm 5.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: T- and B-lymphocyte Subsets by Flow Cytometry - CD56

End point title T- and B-lymphocyte Subsets by Flow Cytometry - CD56

End point description:

Mean and standard deviation results of CD56 lymphocyte subsets is reported. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type Secondary

End point timeframe:

7-10 days after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	9		
Units: Percentage of lymphocytes				
arithmetic mean (standard deviation)	4.6 (\pm 3.4)	6.6 (\pm 5.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: T- and B-lymphocyte Subsets by Flow Cytometry - White Blood Cells

End point title	T- and B-lymphocyte Subsets by Flow Cytometry - White Blood Cells
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End point description:

Mean and standard deviation results of white blood cells subsets is reported. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type	Secondary
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End point timeframe:
pre-dosing (Day 0)

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Cells per 10^3 /UL				
arithmetic mean (standard deviation)	4.19 (\pm 1.49)	3.91 (\pm 1.56)		

Statistical analyses

No statistical analyses for this end point

Secondary: T- and B-lymphocyte Subsets by Flow Cytometry - White Blood Cells

End point title	T- and B-lymphocyte Subsets by Flow Cytometry - White Blood Cells
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End point description:

Mean and standard deviation results of white blood cells subsets is reported. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type	Secondary
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End point timeframe:
7-10 days after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	8		
Units: Cells per 10^3 /UL				
arithmetic mean (standard deviation)	3.24 (\pm 1.10)	4.05 (\pm 1.33)		

Statistical analyses

No statistical analyses for this end point

Secondary: T- and B-lymphocyte Subsets by Flow Cytometry - Lymphocytes

End point title	T- and B-lymphocyte Subsets by Flow Cytometry - Lymphocytes
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End point description:

Mean and standard deviation results of lymphocytes subsets is reported. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type	Secondary
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End point timeframe:
pre-dosing (Day 0)

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Percentage of lymphocytes				
arithmetic mean (standard deviation)	17.62 (\pm 7.56)	27.56 (\pm 9.25)		

Statistical analyses

No statistical analyses for this end point

Secondary: T- and B-lymphocyte Subsets by Flow Cytometry - Lymphocytes

End point title	T- and B-lymphocyte Subsets by Flow Cytometry - Lymphocytes
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End point description:

Mean and standard deviation results of lymphocytes subsets is reported. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type	Secondary
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End point timeframe:
7-10 days after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	8		
Units: Percentage of lymphocytes				
arithmetic mean (standard deviation)	22.58 (\pm 11.89)	23.13 (\pm 8.23)		

Statistical analyses

No statistical analyses for this end point

Secondary: T- and B-lymphocyte Subsets by Flow Cytometry - Absolute Lymphocytes

End point title	T- and B-lymphocyte Subsets by Flow Cytometry - Absolute Lymphocytes
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End point description:

Mean and standard deviation results of absolute lymphocytes subsets is reported. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type	Secondary
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End point timeframe:
pre-dosing (Day 0)

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Cells per $10^3/UL$				
arithmetic mean (standard deviation)	0.77 (\pm 0.51)	1.03 (\pm 0.50)		

Statistical analyses

No statistical analyses for this end point

Secondary: T- and B-lymphocyte Subsets by Flow Cytometry - Absolute Lymphocytes

End point title	T- and B-lymphocyte Subsets by Flow Cytometry - Absolute Lymphocytes
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End point description:

Mean and standard deviation results of absolute lymphocytes subsets is reported. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type	Secondary
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End point timeframe:
7-10 days after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	8		
Units: Cells per 10 ³ /UL				
arithmetic mean (standard deviation)	0.77 (± 0.58)	0.98 (± 0.57)		

Statistical analyses

No statistical analyses for this end point

Secondary: T- and B-lymphocyte Subsets by Flow Cytometry - Absolute Neutrophils

End point title	T- and B-lymphocyte Subsets by Flow Cytometry - Absolute Neutrophils
End point description:	Mean and standard deviation results of absolute neutrophils subsets is reported. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.
End point type	Secondary
End point timeframe:	pre-dosing (Day 0)

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	7		
Units: Cells per 10 ³ /UL				
arithmetic mean (standard deviation)	3300.0 (± 1534.6)	2728.6 (± 1162.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Influenza A/H1N1 Immunoglobulin G (IgG)

End point title	Influenza A/H1N1 Immunoglobulin G (IgG)
End point description:	Mean of influenza-specific IgG from nasal swab is reported. Titers of < 1 were assigned the value of 0.5. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.
End point type	Secondary

End point timeframe:
pre-dosing (Day 0)

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Titer				
arithmetic mean (standard deviation)	954.7 (\pm 1245.3)	672.4 (\pm 492.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Influenza A/H1N1 IgG

End point title	Influenza A/H1N1 IgG
End point description:	Mean of influenza-specific IgG from nasal swab is reported. Titers of < 1 were assigned the value of 0.5. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.
End point type	Secondary
End point timeframe:	35-42 days after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Titer				
arithmetic mean (standard deviation)	924.3 (\pm 1207.2)	844.0 (\pm 645.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Influenza A/H3N2 IgG

End point title	Influenza A/H3N2 IgG
End point description:	Mean of influenza-specific IgG from nasal swab is reported. Titers of < 1 were assigned the value of 0.5. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type	Secondary
End point timeframe: pre-dosing (Day 0)	

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Titer				
arithmetic mean (standard deviation)	799.1 (\pm 426.2)	1842.4 (\pm 1989.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Influenza A/H3N2 IgG

End point title	Influenza A/H3N2 IgG
End point description: Mean of influenza-specific IgG from nasal swab is reported. Titers of < 1 were assigned the value of 0.5. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.	
End point type	Secondary
End point timeframe: 35-42 days after study vaccination	

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Titer				
arithmetic mean (standard deviation)	742.9 (\pm 432.2)	1671.9 (\pm 1646.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Influenza B IgG

End point title	Influenza B IgG
End point description: Mean of influenza-specific IgG from nasal swab is reported. Titers of < 1 were assigned the value of 0.5. All randomized participants who received a full dose of study vaccine, had any valid results in the	

evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type	Secondary
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End point timeframe:

pre-dosing (Day 0)

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Titer				
arithmetic mean (standard deviation)	599.1 (\pm 344.2)	638.6 (\pm 334.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Influenza B IgG

End point title	Influenza B IgG
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End point description:

Mean of influenza-specific IgG from nasal swab is reported. Titers of < 1 were assigned the value of 0.5. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type	Secondary
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End point timeframe:

35-42 days after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Titer				
arithmetic mean (standard deviation)	620.2 (\pm 472.8)	1020.3 (\pm 715.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Influenza A/H1N1 Immunoglobulin M (IgM)

End point title	Influenza A/H1N1 Immunoglobulin M (IgM)
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End point description:

Mean of influenza-specific IgM from nasal swab is reported. Titers of < 1 were assigned the value of 0.5. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type Secondary

End point timeframe:
pre-dosing (Day 0)

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Titer				
arithmetic mean (standard deviation)	150.1 (± 107.0)	160.4 (± 105.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Influenza A/H1N1 IgM

End point title Influenza A/H1N1 IgM

End point description:

Mean of influenza-specific IgM from nasal swab is reported. Titers of < 1 were assigned the value of 0.5. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type Secondary

End point timeframe:

35-42 days after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Titer				
arithmetic mean (standard deviation)	171.3 (± 106.7)	134.8 (± 100.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Influenza A/H3N2 IgM

End point title	Influenza A/H3N2 IgM
End point description: Mean of influenza-specific IgM from nasal swab is reported. Titers of < 1 were assigned the value of 0.5. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.	
End point type	Secondary
End point timeframe: pre-dosing (Day 0)	

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Titer				
arithmetic mean (standard deviation)	153.1 (± 109.4)	134.7 (± 100.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Influenza A/H3N2 IgM

End point title	Influenza A/H3N2 IgM
End point description: Mean of influenza-specific IgM from nasal swab is reported. Titers of < 1 were assigned the value of 0.5. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.	
End point type	Secondary
End point timeframe: 35-42 days after study vaccination	

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Titer				
arithmetic mean (standard deviation)	189.9 (± 98.5)	136.9 (± 103.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Influenza B IgM

End point title	Influenza B IgM
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End point description:

Mean of influenza-specific IgM from nasal swab is reported. Titers of < 1 were assigned the value of 0.5. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type	Secondary
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End point timeframe:

pre-dosing (Day 0)

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Titer				
arithmetic mean (standard deviation)	69.3 (± 61.0)	72.2 (± 66.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Influenza B IgM

End point title	Influenza B IgM
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End point description:

Mean of influenza-specific IgM from nasal swab is reported. Titers of < 1 were assigned the value of 0.5. All randomized participants who received a full dose of study vaccine, had any valid results in the evaluation of immune response, had no protocol deviations, and had sample available for the specified day were analysed for this end point.

End point type	Secondary
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End point timeframe:

35-42 days after study vaccination

End point values	Placebo	FluMist		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10	9		
Units: Titer				
arithmetic mean (standard deviation)	82.0 (± 69.7)	68.4 (± 55.3)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) were collected from the time of investigational product administration through Day 42. Serious adverse events (SAEs) were collected from the time of study drug administration through Day 180.

Adverse event reporting additional description:

Participants who received any study vaccine and had any follow-up for REs and/or AEs were analysed for AEs and SAEs.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	11.0
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Reporting groups

Reporting group title	Placebo
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Reporting group description:

Placebo intranasal mist was composed of allantoic fluid stabilized with buffer containing sucrose, potassium phosphate, and monosodium glutamate. The total volume of 0.5 mL was administered intranasally with a spray applicator (approximately 0.25 mL into each nostril).

Reporting group title	FluMist
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Reporting group description:

The total volume of 0.5 mL of FluMist was administered intranasally with a spray applicator (approximately 0.25 mL into each nostril). Each dose contained approximately 10^7 TCID₅₀ (median tissue culture infectious dose) of each of three influenza virus strains.

Serious adverse events	Placebo	FluMist	
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 10 (30.00%)	1 / 10 (10.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	2 / 10 (20.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			

Bacteraemia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Placebo	FluMist	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 10 (90.00%)	5 / 10 (50.00%)	
Injury, poisoning and procedural complications			
Animal scratch			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Ankle fracture			
subjects affected / exposed	0 / 10 (0.00%)	1 / 10 (10.00%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Conjunctivitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 10 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			

Abdominal pain upper subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0	
Constipation subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1	
Diarrhoea subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0	
Dyspepsia subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0	
Nausea subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0	
Oral pain subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0	
Reproductive system and breast disorders Dysmenorrhoea subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 2	0 / 10 (0.00%) 0	
Respiratory, thoracic and mediastinal disorders Epistaxis subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0	
Sneezing subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0	
Skin and subcutaneous tissue disorders Dermatitis contact subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1	
Dry skin subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0	

Hypoaesthesia facial subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1	
Rash subjects affected / exposed occurrences (all)	2 / 10 (20.00%) 2	0 / 10 (0.00%) 0	
Skin chapped subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0	
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	1 / 10 (10.00%) 1	
Insomnia subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1	
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1	
Musculoskeletal and connective tissue disorders Flank pain subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0	
Pain in extremity subjects affected / exposed occurrences (all)	0 / 10 (0.00%) 0	1 / 10 (10.00%) 1	
Infections and infestations Fungal skin infection subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0	
Metabolism and nutrition disorders Oral intake reduced subjects affected / exposed occurrences (all)	1 / 10 (10.00%) 1	0 / 10 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 March 2005	<ul style="list-style-type: none">• The number of study sites was increased. The isolation procedures specific to St. Jude's were modified to reflect those recommended by the Advisory Committee on Immunization Practices, to accommodate procedures across multiple study sites. The reporting period of significant new medical conditions was clarified.• The exclusion criteria were clarified and/or modified to accommodate participants/regimens across multiple study sites. Specifically, the exclusion criterion for cluster of differentiation 4 (CD4) + T-cell count < 500 cells/mm³ was revised to CD4 + T-cell percentage < 15%; the exclusion criterion for B-cell count < 5% was deleted; and the absolute neutrophil count ANC count ≤ 500 cells/mm³ at screening was revised at study entry.• The screening period was extended to within 16 days before study dosing. Central randomization was implemented with the change to a multiple site study, and the randomization procedures were described. The conditions under which additional participants could be enrolled were added.• The identity and concentration of the influenza virus strains for FluMist study vaccine were revised based on the strains used in the commercially available vaccine during the 2004-2005 influenza season.• The allocation of participants to each treatment group was revised to "approximately" 10 due to the change to a multiple center study.• Collection of radiation therapy with concomitant medication use was added.• The schedule of participant evaluations was revised to accommodate chemotherapy regimens for potential study participants. The reporting period for safety events and the collection procedures for blood samples and nasal specimens were revised or clarified.• Study visits at Days 3 through 5 and Days 17 through 28 were revised to be clinic or at-home visits.• Significant new medical conditions were added as a safety event that would be assessed for severity and for relationship to study vaccine.
08 March 2006	<ul style="list-style-type: none">• Safety information from an immunosuppressed animal model were added.• Safety information for the first four participants vaccinated in the 2005 enrollment period was added.• The Day 17 to 28 visit was revised to occur from Day 14 to 21, with an additional contact on Day 22 to 28, for safety monitoring purposes. Biomarkers for immune response were revised based on actual testing parameters.• Criterion #6 was modified to clarify current status for participants with hematologic malignancy.• Criterion #15 was revised to clarify pregnancy testing. Criterion #19 was modified to have the ANC evaluation be within 24 hours of study entry to possibly avoid multiple blood draws on the same day. Criteria #20 and #21 were combined and modified to exclude only participants who were receiving highdose steroids for ≥ 14 days, which is consistent with the AAP Red Book guidelines for administration of live viral vaccines.• The staggered enrollment schedule was revised to reflect enrollment of the first 4 participants in the 2005 summer enrollment period• The vaccine strains that were to be administered to participants entered during the 2006 enrollment period were updated. The relevant years and influenza seasons were revised to reflect enrollment in a second season. FluMist storage conditions were updated to be consistent with the current labelling.

16 January 2007	<ul style="list-style-type: none">• Information was updated to reflect clinical research use of the refrigerated formulation that had been recently approved. Data from a pivotal pediatric efficacy trial were added.• Safety and shedding data were added for a second pediatric trial in human immunodeficiency virus-infected children. Safety, shedding, and immunogenicity data were added for a post-marketing trial in children and adults.• Updated safety information was provided for the 12 participants who had been enrolled in the first two years of the study. Text was added to reflect target enrollment in 2007 at the end of the 2006-2007 influenza season.• Influenza vaccine strain information was updated for 2007 enrollment.• Pregnancy was added as an immediately reportable event due to the age of the participants eligible for this study.
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Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported