Clinical trial results:
A Randomized, Double-blind, Active Controlled Study to Evaluate the Immunogenicity of Quadrivalent LAIV in Children

Summary

EudraCT number	2009-013326-17
Trial protocol	Outside EU/EEA
Global end of trial date	27 December 2010

Results information

Result version number	v1 (current)
This version publication date	31 January 2016
First version publication date	31 January 2016

Trial information

Trial identification

Sponsor protocol code	MI-CP208

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01091246
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	MedImmune, LLC
Sponsor organisation address	One MedImmune Way, Gaithersburg, United States, MD 20878
Public contact	Clinical Trial Enquiries, MedImmune, LLC, clinicaltrialenquiries@medimmune.com
Scientific contact	Raburn Mallory, Sr Director Clinical Development, MedImmune, LLC, RaburnM@MedImmune.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001051-PIP01-10
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	27 December 2010
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	27 December 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to demonstrate the immunologic non-inferiority of quadrivalent live, attenuated influenza vaccine (MEDI3250) (Q/LAIV) to FluMist in children 2 to 17 years of age by comparing the post dose strain specific geometric mean titers (GMT) of serum hemagglutination inhibition (HAI) antibody.

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Conference on Harmonization guideline E6: Good Clinical Practice. Participating 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	29 March 2010
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	United States: 2312
Worldwide total number of subjects	2312
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)	1993

Adolescents (12-17 years)	319
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 2,481 participants provided written informed consent and were screened for the study. Of these, 2,312 participants were randomized into the study between 29Mar2010 to 12May2010 at 97 sites in the USA.

Pre-assignment

Screening details:

Eligible participants were randomized in a 3:1:1 ratio to receive Q/LAIV, FluMist/B/Yamagata, or FluMist/B/Victoria. Randomization was stratified by age (2 to 8 years, 9 to 17 years). For subjects 2 to 8 years of age only, randomization was also stratified by previous seasonal influenza vaccination history.

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, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Q/LAIV (MEDI3250)

Arm description:

Q/LAIV (quadrivalent live attenuated influenza vaccine) (MEDI3250) was supplied in the Becton Dickinson (BD) Accuspray device that delivers a 0.2 mL total volume intranasal dose divided into each nostril (ie, administered as 0.1 mL per nostril). Each 0.2 mL dose contained 10^7.0 ± 0.5 fluorescent focus units (FFU) of each of 4 temperature sensitive, cold-adapted, attenuated, 6:2 resassortant influenza strains (A/H1N1 [A/South Dakota/6/2007], A/H3N2 [A/Uruguay/716/2007], B/Victoria [B/Malaysia/2506/2004], and B/Yamagata [B/Florida/4/2006]).

Arm type	Experimental
Investigational medicinal product name	MEDI3250
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray, suspension
Routes of administration	Nasal use

Dosage and administration details:

Q/LAIV (quadrivalent live attenuated influenza vaccine) (MEDI3250) was supplied in the Becton Dickinson (BD) Accuspray device that delivers a 0.2 mL total volume intranasal dose divided into each nostril (ie, administered as 0.1 mL per nostril). Each 0.2 mL dose contained 10^7.0 ± 0.5 fluorescent focus units (FFU) of each of 4 temperature sensitive, cold-adapted, attenuated, 6:2 resassortant influenza strains (A/H1N1 [A/South Dakota/6/2007], A/H3N2 [A/Uruguay/716/2007], B/Victoria [B/Malaysia/2506/2004], and B/Yamagata [B/Florida/4/2006]).

Arm title	FluMist/B/Yamagata

Arm description:

FluMist/B/Yamagata (trivalent live attenuated influenza vaccine) was supplied in the BD Accuspray device that delivers a 0.2 mL total volume intranasal dose divided into each nostril (ie, administered as 0.1 mL per nostril). Each 0.2 mL dose contained 10^7.0 ± 0.5 FFU of each of 3 temperature sensitive, cold-adapted, attenuated, 6:2 reassortant influenza strains (A/H1N1 [South Dakota/6/2007], A/H3N2 [A/Uruguay/716/2007], and B/Yamagata [B/Florida/4/2006]).

Arm type	Active comparator

Investigational medicinal product name	FluMist-Y
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray, suspension
Routes of administration	Nasal use

Dosage and administration details:

FluMist/B/Yamagata (trivalent live attenuated influenza vaccine) was supplied in the BD Accuspray device that delivers a 0.2 mL total volume intranasal dose divided into each nostril (ie, administered as 0.1 mL per nostril). Each 0.2 mL dose contained 10^7.0 ± 0.5 FFU of each of 3 temperature sensitive, cold-adapted, attenuated, 6:2 reassortant influenza strains (A/H1N1 [South Dakota/6/2007], A/H3N2 [A/Uruguay/716/2007], and B/Yamagata [B/Florida/4/2006]).

Arm title	FluMist/B/Victoria

Arm description:

FluMist/B/Victoria (trivalent live attenuated influenza vaccine) was supplied in the BD Accuspray device that delivers a 0.2 mL total volume intranasal dose divided into each nostril (ie, administered as 0.1 mL per nostril). Each 0.2 mL dose contained 10^7.0 ± 0.5 FFU of each of 3 temperature sensitive, cold-adapted, attenuated, 6:2 reassortant influenza stains (A/H1N1 [A/South Dakota/6/2007], A/H3N2 [A/Uruguay/716/2007], and B/Victoria [B/Malaysia/2506/2004]).

Arm type	Active comparator
Investigational medicinal product name	FluMist-V
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray, suspension
Routes of administration	Nasal use

Dosage and administration details:

FluMist/B/Victoria (trivalent live attenuated influenza vaccine) was supplied in the BD Accuspray device that delivers a 0.2 mL total volume intranasal dose divided into each nostril (ie, administered as 0.1 mL per nostril). Each 0.2 mL dose contained 10^7.0 ± 0.5 FFU of each of 3 temperature sensitive, cold-adapted, attenuated, 6:2 reassortant influenza stains (A/H1N1 [A/South Dakota/6/2007], A/H3N2 [A/Uruguay/716/2007], and B/Victoria [B/Malaysia/2506/2004]).

Number of subjects in period 1	Q/LAIV (MEDI3250)	FluMist/B/Yamagata	FluMist/B/Victoria
Started	1385	464	463
Completed	1350	448	450
Not completed	35	16	13
Consent withdrawn by subject	9	5	4
Subject not dosed	2	-	1
Adverse event, non-fatal	1	-	1
Lost to follow-up	23	11	7

Baseline characteristics

Reporting groups	
Reporting group title	Q/LAIV (MEDI3250)
Reporting group description:	
Q/LAIV (quadrivalent live attenuated influenza vaccine) (MEDI3250) was supplied in the Becton Dickinson (BD) Accuspray device that delivers a 0.2 mL total volume intranasal dose divided into each nostril (ie, administered as 0.1 mL per nostril). Each 0.2 mL dose contained 10^7.0 ± 0.5 fluorescent focus units (FFU) of each of 4 temperature sensitive, cold-adapted, attenuated, 6:2 resassortant influenza strains (A/H1N1 [A/South Dakota/6/2007], A/H3N2 [A/Uruguay/716/2007], B/Victoria [B/Malaysia/2506/2004], and B/Yamagata [B/Florida/4/2006]).	
Reporting group title	FluMist/B/Yamagata
Reporting group description:	
FluMist/B/Yamagata (trivalent live attenuated influenza vaccine) was supplied in the BD Accuspray device that delivers a 0.2 mL total volume intranasal dose divided into each nostril (ie, administered as 0.1 mL per nostril). Each 0.2 mL dose contained 10^7.0 ± 0.5 FFU of each of 3 temperature sensitive, cold-adapted, attenuated, 6:2 reassortant influenza strains (A/H1N1 [South Dakota/6/2007], A/H3N2 [A/Uruguay/716/2007], and B/Yamagata [B/Florida/4/2006]).	
Reporting group title	FluMist/B/Victoria
Reporting group description:	
FluMist/B/Victoria (trivalent live attenuated influenza vaccine) was supplied in the BD Accuspray device that delivers a 0.2 mL total volume intranasal dose divided into each nostril (ie, administered as 0.1 mL per nostril). Each 0.2 mL dose contained 10^7.0 ± 0.5 FFU of each of 3 temperature sensitive, cold-adapted, attenuated, 6:2 reassortant influenza stains (A/H1N1 [A/South Dakota/6/2007], A/H3N2 [A/Uruguay/716/2007], and B/Victoria [B/Malaysia/2506/2004]).	

Reporting group values	Q/LAIV (MEDI3250)	FluMist/B/Yamagata	FluMist/B/Victoria
Number of subjects	1385	464	463
Age categorical Units: Subjects			
Age Continuous | Units: years			
arithmetic mean	6.7	6.8	6.8
standard deviation	± 3.8	± 3.8	± 3.9
Gender, Male/Female Units: participants			
Female	707	229	240
Male	678	235	223

Reporting group values	Total		
Number of subjects	2312		
Age categorical Units: Subjects			
Age Continuous | Units: years arithmetic mean standard deviation	-		
Gender, Male/Female Units: participants			
Female	1176		

Male	1136		

End points

End points reporting groups

Reporting group title	Q/LAIV (MEDI3250)

Reporting group description:

Q/LAIV (quadrivalent live attenuated influenza vaccine) (MEDI3250) was supplied in the Becton Dickinson (BD) Accuspray device that delivers a 0.2 mL total volume intranasal dose divided into each nostril (ie, administered as 0.1 mL per nostril). Each 0.2 mL dose contained 10^7.0 ± 0.5 fluorescent focus units (FFU) of each of 4 temperature sensitive, cold-adapted, attenuated, 6:2 resassortant influenza strains (A/H1N1 [A/South Dakota/6/2007], A/H3N2 [A/Uruguay/716/2007], B/Victoria [B/Malaysia/2506/2004], and B/Yamagata [B/Florida/4/2006]).

Reporting group title	FluMist/B/Yamagata

Reporting group description:

FluMist/B/Yamagata (trivalent live attenuated influenza vaccine) was supplied in the BD Accuspray device that delivers a 0.2 mL total volume intranasal dose divided into each nostril (ie, administered as 0.1 mL per nostril). Each 0.2 mL dose contained 10^7.0 ± 0.5 FFU of each of 3 temperature sensitive, cold-adapted, attenuated, 6:2 reassortant influenza strains (A/H1N1 [South Dakota/6/2007], A/H3N2 [A/Uruguay/716/2007], and B/Yamagata [B/Florida/4/2006]).

Reporting group title	FluMist/B/Victoria

Reporting group description:

FluMist/B/Victoria (trivalent live attenuated influenza vaccine) was supplied in the BD Accuspray device that delivers a 0.2 mL total volume intranasal dose divided into each nostril (ie, administered as 0.1 mL per nostril). Each 0.2 mL dose contained 10^7.0 ± 0.5 FFU of each of 3 temperature sensitive, cold-adapted, attenuated, 6:2 reassortant influenza stains (A/H1N1 [A/South Dakota/6/2007], A/H3N2 [A/Uruguay/716/2007], and B/Victoria [B/Malaysia/2506/2004]).

Subject analysis set title	All FluMist Group: Immunogenicity Population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The Immunogenicity Population included all participants who received any investigational product and had post dose HAI antibody measurement and had no protocol deviation judged to have the potential to interfere with the generation or interpretation of an immune response. All FluMist group for A/H1N1 and A/H3N2 strains, where data from both the FluMist/B/Yamagata arm and the FluMist/B/Victoria arm were combined.

Subject analysis set title	All FluMist Group: A/H1N1
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All FluMist group for A/H1N1 and A/H3N2 strains, where data from both the FluMist/B/Yamagata arm and the FluMist/B/Victoria arm were combined.All participants who received any investigational product (Q=1385; All FM=927), had post dose HAI antibody measurement at the appropriate time, and had no protocol deviation judged to have the potential to interfere with the generation or interpretation of an immune response (Q=1320; All FM=878).

Subject analysis set title	All FluMist Group: A/H3N2
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All FluMist group for A/H1N1 and A/H3N2 strains, where data from both the FluMist/B/Yamagata arm and the FluMist/B/Victoria arm were combined. All participants who received any investigational product (Q=1385; All FM=927), had post dose HAI antibody measurement at the appropriate time, and had no protocol deviation judged to have the potential to interfere with the generation or interpretation of an immune response (Q=1320; All FM=879).

Subject analysis set title	All FluMist Group: Serosusceptible to A/H1N1
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All FluMist group for A/H1N1 and A/H3N2 strains, where data from both the FluMist/B/Yamagata arm and the FluMist/B/Victoria arm were combined. All participants who received any investigational product (Q=1385; All FM=927), had post dose HAI antibody measurement at the appropriate time, had no protocol deviation judged to have the potential to interfere with the generation or interpretation of an immune response, and were serosusceptible to the strain (Q=569; All FM=392).

Subject analysis set title	All FluMist Group: Serosusceptible to A/H3N2
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All FluMist group for A/H1N1 and A/H3N2 strains, where data from both the FluMist/B/Yamagata arm and the FluMist/B/Victoria arm were combined.
All participants who received any investigational product (Q=1385; All FM=927), had post dose HAI antibody measurement at the appropriate time, had no protocol deviation judged to have the potential to interfere with the generation or interpretation of an immune response, and were serosusceptible to the strain (Q=435; All FM=298).

Subject analysis set title	All FluMist Group: Seronegative to A/H1N1
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All FluMist group for A/H1N1 and A/H3N2 strains, where data from both the FluMist/B/Yamagata arm and the FluMist/B/Victoria arm were combined.
All participants who received any investigational product (Q=1385; All FM=927), had post dose HAI antibody measurement at the appropriate time, and had no protocol deviation judged to have the potential to interfere with the generation or interpretation of an immune response and were seronegative to the strain (Q=460; All FM=321).

Subject analysis set title	All FluMist Group: Seronegative to A/H3N2
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All FluMist group for A/H1N1 and A/H3N2 strains, where data from both the FluMist/B/Yamagata arm and the FluMist/B/Victoria arm were combined.
All participants who received any investigational product (Q=1385; All FM=927), had post dose HAI antibody measurement at the appropriate time and had no protocol deviation judged to have the potential to interfere with the generation or interpretation of an immune response and were seronegative to the strain (Q=364; All FM=244).

Subject analysis set title	Post Dose 1 solicited symptoms analyses
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All FluMist group for A/H1N1 and A/H3N2 strains, where data from both the FluMist/B/Yamagata arm and the FluMist/B/Victoria arm were combined. The total number of subjects evaluable for post Dose 1 solicited symptoms analyses (SSA) were reported.

Subject analysis set title	Post-dose 1 solicited symptoms analyses: 2-dose group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All FluMist group for A/H1N1 and A/H3N2 strains, where data from both the FluMist/B/Yamagata arm and the FluMist/B/Victoria arm were combined. The number of subjects evaluable for post Dose 1 solicited symptoms analyses for two-dose group were reported.

Subject analysis set title	Post Dose 2 solicited symptoms analyses
Subject analysis set type	Sub-group analysis

Subject analysis set description:

All FluMist group for A/H1N1 and A/H3N2 strains, where data from both the FluMist/B/Yamagata arm and the FluMist/B/Victoria arm were combined. The total number of subjects evaluable for post Dose 2 solicited symptoms analyses were reported.

Subject analysis set title	All FluMist Group: Safety population
Subject analysis set type	Sub-group analysis

Subject analysis set description:

The Safety Population included all participants who received any investigational product and had safety data available. All FluMist group for A/H1N1 and A/H3N2 strains, where data from both the FluMist/B/Yamagata arm and the FluMist/B/Victoria arm were combined.

Subject analysis set title	Safety population: Two-dose group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who received a different investigational product at Dose 2 than at Dose 1 were excluded from the Safety Population for Dose 2. All FluMist group for A/H1N1 and A/H3N2 strains, where data from both the FluMist/B/Yamagata arm and the FluMist/B/Victoria arm were combined.

Subject analysis set title	Evaluable Safety population: Two-dose group
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants who received a different investigational product at Dose 2 than at Dose 1 were excluded

from the Safety Population for Dose 2. Evaluable subjects of the two-doe group were reported. All FluMist group for A/H1N1 and A/H3N2 strains, where data from both the FluMist/B/Yamagata arm and the FluMist/B/Victoria arm were combined.

Primary: The 4 post-dose strain-specific serum hemagglutination inhibition (HAI) antibody geometric mean titers (GMT) in the Q/LAIV (MEDI3250) arm are noninferior to those in the comparator FluMist group.

End point title	The 4 post-dose strain-specific serum hemagglutination inhibition (HAI) antibody geometric mean titers (GMT) in the Q/LAIV (MEDI3250) arm are noninferior to those in the comparator FluMist group.

End point description:

Non-inferior immune response was defined as having the upper bound of the 2-sided 95% confidence intervals (CIs) for the HAI antibody GMT ratio (FluMist comparator divided by Q/LAIV) ≤ 1.5 for each of the 4 strains. In the below table, '99999' indicates data was not reported since, the comparators for the GMT ratios for the primary endpoint were participants in the All FluMist group (combined data for both FluMist arms) for A/H1N1 and A/H3N2 strains. '88888' indicates data was not reported since B/Yamagata strain not in the investigational product. '77777' indicates data was not reported since B/Victoria strain not in the investigational product. All participants who received any investigational product (Q=1385; FY=464; FV=463; All FM=927), had post dose HAI antibody measurement at the appropriate time and had no protocol deviation judged to have the potential to interfere with the generation or interpretation of an immune response (Q=1327; FY=445; FV=437; All FM=883).

End point type	Primary

End point timeframe:

Day 28 post immunogenicity dose

End point values	Q/LAIV (MEDI3250)	FluMist/B/Yamagata	FluMist/B/Victoria	All FluMist Group: Immunogenicity Population
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	1327	445	437	883
Units: Geometric mean titer				
geometric mean (full range (min-max))				
A/H1N1	16.7 (15.9 to 17.6)	99999 (99999 to 99999)	99999 (99999 to 99999)	17.9 (16.8 to 19.1)
A/H3N2	27.7 (26.1 to 29.4)	99999 (99999 to 99999)	99999 (99999 to 99999)	28.8 (26.7 to 31.1)
B/Yamagata	49.6 (46.6 to 52.8)	59.8 (53.7 to 66.7)	88888 (88888 to 88888)	99999 (99999 to 99999)
B/Victoria	35.4 (33.3 to 37.7)	77777 (77777 to 77777)	37 (33.4 to 41)	99999 (99999 to 99999)

Statistical analyses

Statistical analysis title	Statistical analysis 1

Statistical analysis description:

A/H1N1: The statistical hypothesis testing for the primary endpoint for Q/LAIV was: H0: Rj > 1.5, for any j HA: Rj ≤ 1.5, for all j Where Rj was any of the 4 strain-specific post immunogenicity dose GMT ratios: (FluMist/B/Yamagata + FluMist/B/Victoria) / (Q/LAIV) for A/H1N1 strain

Comparison groups	Q/LAIV (MEDI3250) v All FluMist Group: Immunogenicity Population

Number of subjects included in analysis	2210
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Method	Bootstrapping
Parameter estimate	Ratio of geometric mean
Point estimate	1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.98
upper limit	1.16

Notes:

[1] - The noninferior immune response was assessed by evaluating the upper bound of the two-sided 95% confidence intervals for the strain specific HAI antibody GMT ratios (FluMist divided by Q/LAIV) to the noninferiority margin of 1.5.

Statistical analysis title	Statistical analysis 2

Statistical analysis description:

A/H3N2: The statistical hypothesis testing for the primary endpoint for Q/LAIV was: H0: Rj > 1.5, for any j HA: Rj ≤ 1.5, for all j Where Rj was any of the 4 strain-specific post immunogenicity dose GMT ratios: (FluMist/B/Yamagata + FluMist/B/Victoria) / (Q/LAIV) for A/H3N2 strain

Comparison groups	Q/LAIV (MEDI3250) v All FluMist Group: Immunogenicity Population
Number of subjects included in analysis	2210
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
Method	Bootstrapping
Parameter estimate	Ratio of geometric means
Point estimate	1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.94
upper limit	1.14

Notes:

[2] - The noninferior immune response was assessed by evaluating the upper bound of the two-sided 95% confidence intervals for the strain specific HAI antibody GMT ratios (FluMist divided by Q/LAIV) to the noninferiority margin of 1.5. If the upper bounds of 95% CIs were ≤ 1.5 for all 4 strains, the immunologic noninferiority of Q/LAIV compared to FluMist was declared.

Statistical analysis title	Statistical analysis 3

Statistical analysis description:

B/Yamagata: The statistical hypothesis testing for the primary endpoint for Q/LAIV was: H0: Rj > 1.5, for any j HA: Rj ≤ 1.5, for all j Where Rj was any of the 4 strain-specific post immunogenicity dose GMT ratios: (FluMist/B/Yamagata) / (Q/LAIV) for B/Yamagata strain

Comparison groups	Q/LAIV (MEDI3250) v FluMist/B/Yamagata
Number of subjects included in analysis	1772
Analysis specification	Pre-specified
Analysis type	non-inferiority[3]
Parameter estimate	Ratio of geometric mean
Point estimate	1.21

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.07
upper limit	1.37

Notes:

[3] - The noninferior immune response was assessed by evaluating the upper bound of the two-sided 95% confidence intervals for the strain specific HAI antibody GMT ratios (FluMist divided by Q/LAIV) to the noninferiority margin of 1.5. If the upper bounds of 95% CIs were ≤ 1.5 for all 4 strains, the immunologic noninferiority of Q/LAIV compared to FluMist was declared.

Statistical analysis title	Statistical analysis 4

Statistical analysis description:

B/Victoria: The statistical hypothesis testing for the primary endpoint for Q/LAIV was: H0: Rj > 1.5, for any j HA: Rj ≤ 1.5, for all j Where Rj was any of the 4 strain-specific post immunogenicity dose GMT ratios: (FluMist/B/Victoria) / (Q/LAIV) for B/Victoria strain

Comparison groups	Q/LAIV (MEDI3250) v FluMist/B/Victoria
Number of subjects included in analysis	1764
Analysis specification	Pre-specified
Analysis type	non-inferiority[4]
Parameter estimate	Ratio of geometric mean
Point estimate	1.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.93
upper limit	1.18

Notes:

[4] - The noninferior immune response was assessed by evaluating the upper bound of the two-sided 95% confidence intervals for the strain specific HAI antibody GMT ratios (FluMist divided by Q/LAIV) to the noninferiority margin of 1.5. If the upper bounds of 95% confidence intervals were ≤ 1.5 for all 4 strains, the immunologic noninferiority of Q/LAIV compared to FluMist was declared.

Secondary: The Percent of Participants (Regardless of Serostatus) Within Each Treatment Arm Who Experienced a Seroresponse to the A/H1N1 Strain Post Immunogenicity Dose

End point title	The Percent of Participants (Regardless of Serostatus) Within Each Treatment Arm Who Experienced a Seroresponse to the A/H1N1 Strain Post Immunogenicity Dose[5]

End point description:

Seroresponse was defined as a ≥ 4-fold rise in HAI antibody titer from baseline.
All participants who received any investigational product (Q=1385; All FM=927), had post dose HAI antibody measurement at the appropriate time, and had no protocol deviation judged to have the potential to interfere with the generation or interpretation of an immune response (Q=1320; All FM=878).

End point type	Secondary

End point timeframe:

Day 0 and Day 28 post immunogenicity dose

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was related to these respective arms only, hence not reporting statistics for all the arms in the baseline period.

End point values	Q/LAIV (MEDI3250)	All FluMist Group: A/H1N1		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	1320	878		
Units: percent of participants				
number (not applicable)	6.3	8.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Participants (Regardless of Serostatus) Within Each Treatment Arm Who Experienced a Seroresponse to the A/H3N2 Strain Post Immunogenicity Dose

End point title	Percent of Participants (Regardless of Serostatus) Within Each Treatment Arm Who Experienced a Seroresponse to the A/H3N2 Strain Post Immunogenicity Dose[6]

End point description:

Seroresponse was defined as a ≥ 4-fold rise in HAI antibody titer from baseline.
All participants who received any investigational product (Q=1385; All FM=927), had post dose HAI antibody measurement at the appropriate time and had no protocol deviation judged to have the potential to interfere with the generation or interpretation of an immune response (Q=1321; All FM=879).

End point type	Secondary

End point timeframe:

Day 0 and Day 28 post immunogenicity dose

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was related to these respective arms only, hence not reporting statistics for all the arms in the baseline period.

End point values	Q/LAIV (MEDI3250)	All FluMist Group: A/H3N2		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	1321	879		
Units: Percent of participants				
number (not applicable)	3.9	3.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Participants (Regardless of Serostatus) Within Each Treatment Arm Who Experienced a Seroresponse to the B/Yamagata Strain Post Immunogenicity Dose

End point title	Percent of Participants (Regardless of Serostatus) Within Each Treatment Arm Who Experienced a Seroresponse to the B/Yamagata Strain Post Immunogenicity Dose[7]

End point description:

Seroresponse was defined as a ≥ 4-fold rise in HAI antibody titer from baseline.
All participants who received any investigational product (Q=1385; FY=464), had post dose HAI antibody measurement at the appropriate time, and had no protocol deviation judged to have the potential to interfere with the generation or interpretation of an immune response (Q=1321; FY=441).

End point type	Secondary

End point timeframe:

Day 0 and Day 28 post immunogenicity dose

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was related to these respective arms only, hence not reporting statistics for all the arms in the baseline period.

End point values	Q/LAIV (MEDI3250)	FluMist/B/Yamagata		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1321	441		
Units: Percent of participants				
number (not applicable)	43.4	44.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Participants (Regardless of Serostatus) Within Each Treatment Arm Who Experienced a Seroresponse to the B/Victoria Strain Post Immunogenicity Dose

End point title	Percent of Participants (Regardless of Serostatus) Within Each Treatment Arm Who Experienced a Seroresponse to the B/Victoria Strain Post Immunogenicity Dose[8]

End point description:

Seroresponse was defined as a ≥ 4-fold rise from baseline.
All participants who received any investigational product (Q=1385; FV=463), had post dose HAI antibody measurement at the appropriate time, and had no protocol deviation judged to have the potential to interfere with the generation or interpretation of an immune response (Q=1321; FV=437).

End point type	Secondary

End point timeframe:

Day 0 and Day 28 post immunogenicity dose

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was related to these respective arms only, hence not reporting statistics for all the arms in the baseline period.

End point values	Q/LAIV (MEDI3250)	FluMist/B/Victoria		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1321	437		
Units: Percent of participants				
number (not applicable)	39.1	38.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Serosusceptible Participants Within Each Treatment Arm Who Experienced a Seroresponse to the A/H1N1 Strain Post Immunogenicity Dose

End point title	Percent of Serosusceptible Participants Within Each Treatment Arm Who Experienced a Seroresponse to the A/H1N1 Strain Post Immunogenicity Dose[9]

End point description:

Serosusceptible was defined as a baseline HAI titer ≤ 8. Seroresponse was defined as a ≥ 4-fold rise in HAI titer from baseline.
All participants who received any investigational product (Q=1385; All FM=927), had post dose HAI antibody measurement at the appropriate time, had no protocol deviation judged to have the potential to interfere with the generation or interpretation of an immune response, and were serosusceptible to the strain (Q=569; All FM=392).

End point type	Secondary

End point timeframe:

Day 0 and Day 28 post immunogenicity dose

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was related to these respective arms only, hence not reporting statistics for all the arms in the baseline period.

End point values	Q/LAIV (MEDI3250)	All FluMist Group: Serosusceptible to A/H1N1		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	569	392		
Units: Percent of participants				
number (not applicable)	12.7	17.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Serosusceptible Participants Within Each Treatment Arm Who Experience Seroresponse to the A/H3N2 Strain Post Immunogenicity Dose

End point title	Percent of Serosusceptible Participants Within Each Treatment Arm Who Experience Seroresponse to the A/H3N2 Strain Post Immunogenicity Dose[10]

End point description:

Serosusceptible was defined as a baseline HAI titer ≤ 8. Seroresponse was defined as a ≥ 4-fold rise in HAI titer from baseline. All participants who received any investigational product (Q=1385; All FM=927), had post dose HAI antibody measurement at the appropriate time, had no protocol deviation judged to have the potential to interfere with the generation or interpretation of an immune response, and were serosusceptible to the strain (Q=435; All FM=298).

End point type	Secondary

End point timeframe:

Day 0 and Day 28 post immunogenicity dose

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was related to these respective arms only, hence not reporting statistics for all the arms in the baseline period.

End point values	Q/LAIV (MEDI3250)	All FluMist Group: Serosusceptible to A/H3N2		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	435	298		
Units: Percent of participants				
number (not applicable)	9.9	9.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Serosusceptible Participants Within Each Treatment Arm Who Experience Seroresponse to the B/Yamagata Strain Post Immunogenicity Dose

End point title	Percent of Serosusceptible Participants Within Each Treatment Arm Who Experience Seroresponse to the B/Yamagata Strain Post Immunogenicity Dose[11]

End point description:

Serosusceptible was defined as a baseline HAI titer ≤ 8. Seroresponse was defined as a ≥ 4-fold rise in HAI titer from baseline.
All participants who received any investigational product (Q=1385; FY=464), had post dose HAI antibody measurement at the appropriate time, had no protocol deviation judged to have the potential to interfere with the generation or interpretation of an immune response, and were serosusceptible to the strain (Q=588; FY=192).

End point type	Secondary

End point timeframe:

Day 0 and Day 28 post immunogenicity dose

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was related to these respective arms only, hence not reporting statistics for all the arms in the baseline period.

End point values	Q/LAIV (MEDI3250)	FluMist/B/Yamagata		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	588	192		
Units: Percent of participants				
number (not applicable)	79.1	81.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Serosusceptible Participants Within Each Treatment Arm Who Experience Seroresponse to the B/Victoria Strain Post Immunogenicity Dose

End point title	Percent of Serosusceptible Participants Within Each Treatment Arm Who Experience Seroresponse to the B/Victoria Strain Post Immunogenicity Dose[12]

End point description:

Serosusceptible was defined as a baseline HAI titer ≤ 8. Seroresponse was defined as a ≥ 4-fold rise in HAI titer from baseline.
All participants who received any investigational product (Q=1385; FV=463), had post dose HAI antibody measurement at the appropriate time, had no protocol deviation judged to have the potential to interfere with the generation or interpretation of an immune response, and were serosusceptible to the strain (Q=620; FV=191).

End point type	Secondary

End point timeframe:

Day 0 and Day 28 post immunogenicity dose

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was related to these respective arms only, hence not reporting statistics for all the arms in the baseline period.

End point values	Q/LAIV (MEDI3250)	FluMist/B/Victoria		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	620	191		
Units: Percent of participants				
number (not applicable)	66.1	69.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Seronegative Participants Within Each Treatment Arm Who Experienced a Seroresponse to the A/H1N1 Strain Post Immunogenicity Dose

End point title	Percent of Seronegative Participants Within Each Treatment Arm Who Experienced a Seroresponse to the A/H1N1 Strain Post Immunogenicity Dose[13]

End point description:

Seronegative was defined as a baseline HAI titer ≤ 4. Seroresponse was defined as a ≥ 4-fold rise in HAI titer from baseline.
All participants who received any investigational product (Q=1385; All FM=927), had post dose HAI antibody measurement at the appropriate time, and had no protocol deviation judged to have the potential to interfere with the generation or interpretation of an immune response and were seronegative to the strain (Q=460; All FM=321).

End point type	Secondary

End point timeframe:

Day 0 and Day 28 post immunogenicity dose

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was related to these respective arms only, hence not reporting statistics for all the arms in the baseline period.

End point values	Q/LAIV (MEDI3250)	All FluMist Group: Seronegative to A/H1N1		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	460	321		
Units: Percent of participants				
number (not applicable)	14.6	19.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Seronegative Participants Within Each Treatment Arm Who Experienced a Seroresponse to the A/H3N2 Strain Post Immunogenicity Dose

End point title	Percent of Seronegative Participants Within Each Treatment Arm Who Experienced a Seroresponse to the A/H3N2 Strain Post Immunogenicity Dose[14]

End point description:

Seronegative was defined as a baseline HAI titer ≤ 4. Seroresponse was defined as a ≥ 4-fold rise in HAI titer from baseline.
All participants who received any investigational product (Q=1385; All FM=927), had post dose HAI antibody measurement at the appropriate time and had no protocol deviation judged to have the potential to interfere with the generation or interpretation of an immune response and were seronegative to the strain (Q=364; All FM=244).

End point type	Secondary

End point timeframe:

Day 0 and Day 28 post immunogenicity dose

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was related to these respective arms only, hence not reporting statistics for all the arms in the baseline period.

End point values	Q/LAIV (MEDI3250)	All FluMist Group: Seronegative to A/H3N2		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	364	244		
Units: Percent of participants				
number (not applicable)	9.9	11.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Seronegative Participants Within Each Treatment Arm Who Experienced a Seroresponse to the B/Yamagata Strain Post Immunogenicity Dose

End point title	Percent of Seronegative Participants Within Each Treatment Arm Who Experienced a Seroresponse to the B/Yamagata Strain Post Immunogenicity Dose[15]

End point description:

Seronegative was defined as a baseline HAI titer ≤ 4. Seroresponse was defined as a ≥ 4-fold rise in HAI titer from baseline.
All participants who received any investigational product (Q=1385; FY=464), had post dose HAI antibody measurement at the appropriate time, had no protocol deviation judged to have the potential to interfere with the generation or interpretation of an immune response, and were seronegative to the strain (Q=483; FY=165).

End point type	Secondary

End point timeframe:

Day 0 and Day 28 post immunogenicity dose

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was related to these respective arms only, hence not reporting statistics for all the arms in the baseline period.

End point values	Q/LAIV (MEDI3250)	FluMist/B/Yamagata		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	483	165		
Units: Percent of participants				
number (not applicable)	83	84.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Seronegative Participants Within Each Treatment Arm Who Experienced a Seroresponse to the B/Victoria Strain Post Immunogenicity Dose

End point title	Percent of Seronegative Participants Within Each Treatment Arm Who Experienced a Seroresponse to the B/Victoria Strain

	Post Immunogenicity Dose[16]

End point description:

Seronegative was defined as a baseline HAI titer ≤ 4. Seroresponse was defined as a ≥ 4-fold rise in HAI titer from baseline.
All participants who received any investigational product (Q=1385; FV=463), had post dose HAI antibody measurement at the appropriate time, had no protocol deviation judged to have the potential to interfere with the generation or interpretation of an immune response, and were seronegative to the strain (Q=487; FV=159).

End point type	Secondary

End point timeframe:

Day 0 and Day 28 post immunogenicity dose

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was related to these respective arms only, hence not reporting statistics for all the arms in the baseline period.

End point values	Q/LAIV (MEDI3250)	FluMist/B/Victoria		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	487	159		
Units: Percent of participants				
number (not applicable)	68.8	73.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Participants (Regardless of Serostatus) Who Achieved an A/H1N1 or A/H3N2 Strain-specific HAI Antibody Titer ≥ 32 Post Immunogenicity Dose

End point title	Percent of Participants (Regardless of Serostatus) Who Achieved an A/H1N1 or A/H3N2 Strain-specific HAI Antibody Titer ≥ 32 Post Immunogenicity Dose[17]

End point description:

All participants who received any investigational product (Q=1385; All FM=927), had post dose HAI antibody measurement at the appropriate time, and had no protocol deviation judged to have the potential to interfere with the generation or interpretation of an immune response (Q=1327; All FM=883).

End point type	Secondary

End point timeframe:

Day 28 post immunogenicity dose

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was related to these respective arms only, hence not reporting statistics for all the arms in the baseline period.

End point values	Q/LAIV (MEDI3250)	All FluMist Group: Immunogenicity Population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	1327	883		
Units: Percent of participants				
number (not applicable)				
A/H1N1	43.1	43.8		
A/H3N2	55.7	55.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Participants (Regardless of Serostatus) Who Achieved a B/Yamagata HAI Antibody Titer ≥ 32 Post Immunogenicity Dose

End point title	Percent of Participants (Regardless of Serostatus) Who Achieved a B/Yamagata HAI Antibody Titer ≥ 32 Post Immunogenicity Dose[18]

End point description:

All participants who received any investigational product (Q=1385; FY=464), had post dose HAI antibody measurement at the appropriate time, and had no protocol deviation judged to have the potential to interfere with the generation or interpretation of an immune response (Q=1327; FY=445).

End point type	Secondary

End point timeframe:

Day 28 post immunogenicity dose

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was related to these respective arms only, hence not reporting statistics for all the arms in the baseline period.

End point values	Q/LAIV (MEDI3250)	FluMist/B/Yamagata		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1327	445		
Units: Percent of participants				
number (not applicable)	76.5	81.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Participants (Regardless of Serostatus) Who Achieved a B/Victoria HAI Antibody Titer ≥ 32 Post Immunogenicity Dose

End point title	Percent of Participants (Regardless of Serostatus) Who Achieved a B/Victoria HAI Antibody Titer ≥ 32 Post Immunogenicity Dose[19]

End point description:

All participants who received any investigational product (Q=1385; FV=463), had post dose HAI antibody measurement at the appropriate time, and had no protocol deviation judged to have the potential to interfere with the generation or interpretation of an immune response (Q=1327; FV=437).

End point type	Secondary

End point timeframe:

Day 28 post immunogenicity dose

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was related to these respective arms only, hence not reporting statistics for all the arms in the baseline period.

End point values	Q/LAIV (MEDI3250)	FluMist/B/Victoria		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1327	437		
Units: Percent of participants				
number (not applicable)	65.6	66.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Serosusceptible Participants Who Achieved an A/H1N1 HAI Antibody Titer ≥ 32 Post Immunogenicity Dose

End point title	Percent of Serosusceptible Participants Who Achieved an A/H1N1 HAI Antibody Titer ≥ 32 Post Immunogenicity Dose[20]

End point description:

Serosusceptible was defined as a baseline HAI titer ≤ 8.

End point type	Secondary

End point timeframe:

Day 28 post immunogenicity dose

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was related to these respective arms only, hence not reporting statistics for all the arms in the baseline period.

End point values	Q/LAIV (MEDI3250)	All FluMist Group: Serosusceptible to A/H1N1		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	569	392		
Units: Percent of participants				
number (not applicable)	5.1	6.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Serosusceptible Participants Who Achieved an A/H3N2 HAI Antibody Titer ≥ 32 Post Immunogenicity Dose

End point title	Percent of Serosusceptible Participants Who Achieved an A/H3N2 HAI Antibody Titer ≥ 32 Post Immunogenicity Dose[21]

End point description:

Serosusceptible was defined as a baseline HAI titer ≤ 8.
All participants who received any investigational product (Q=1385; All FM=927), had post dose HAI antibody measurement at the appropriate time, had no protocol deviation judged to have the potential to interfere with the generation or interpretation of an immune response, and were serosusceptible to the strain (Q=569; All FM=392).

End point type	Secondary

End point timeframe:

Day 28 post immunogenicity dose

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was related to these respective arms only, hence not reporting statistics for all the arms in the baseline period.

End point values	Q/LAIV (MEDI3250)	All FluMist Group: Serosusceptible to A/H3N2		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	435	298		
Units: Percent of participants				
number (not applicable)	4.8	4.4		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Serosusceptible Participants Who Achieved a B/Yamagata HAI Antibody Titer ≥ 32 Post Immunogenicity Dose

End point title	Percent of Serosusceptible Participants Who Achieved a B/Yamagata HAI Antibody Titer ≥ 32 Post Immunogenicity Dose[22]

End point description:

Serosusceptible was defined as a baseline HAI titer ≤ 8.
All participants who received any investigational product (Q=1385; All FM=927), had post dose HAI antibody measurement at the appropriate time, had no protocol deviation judged to have the potential

to interfere with the generation or interpretation of an immune response, and were serosusceptible to the strain (Q=435; All FM=298).

End point type	Secondary

End point timeframe:

Day 28 post immunogenicity dose

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was related to these respective arms only, hence not reporting statistics for all the arms in the baseline period.

End point values	Q/LAIV (MEDI3250)	FluMist/B/Yamagata		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	588	192		
Units: Percent of participants				
number (not applicable)	60.9	69.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Serosusceptible Participants Who Achieved a B/Victoria HAI Antibody Titer ≥ 32 Post Immunogenicity Dose

End point title	Percent of Serosusceptible Participants Who Achieved a B/Victoria HAI Antibody Titer ≥ 32 Post Immunogenicity Dose[23]

End point description:

Serosusceptible was defined as a baseline HAI titer ≤ 8. All participants who received any investigational product (Q=1385; FY=464), had post dose HAI antibody measurement at the appropriate time, had no protocol deviation judged to have the potential to interfere with the generation or interpretation of an immune response, and were serosusceptible to the strain (Q=588; FY=192).

End point type	Secondary

End point timeframe:

Day 28 post immunogenicity dose

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was related to these respective arms only, hence not reporting statistics for all the arms in the baseline period.

End point values	Q/LAIV (MEDI3250)	FluMist/B/Victoria		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	620	191		
Units: Percent of participants				
number (not applicable)	41.1	44		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Seronegative Participants Who Achieved an A/H1N1 HAI Antibody Titer ≥ 32 Post Immunogenicity Dose

End point title	Percent of Seronegative Participants Who Achieved an A/H1N1 HAI Antibody Titer ≥ 32 Post Immunogenicity Dose[24]

End point description:

Seronegative was defined as a baseline HAI titer ≤ 4. All participants who received any investigational product (Q=1385; FV=463), had post dose HAI antibody measurement at the appropriate time, had no protocol deviation judged to have the potential to interfere with the generation or interpretation of an immune response, and were serosusceptible to the strain (Q=620; FV=191).

End point type	Secondary

End point timeframe:

Day 28 post immunogenicity dose

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was related to these respective arms only, hence not reporting statistics for all the arms in the baseline period.

End point values	Q/LAIV (MEDI3250)	All FluMist Group: Seronegative to A/H1N1		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	460	321		
Units: Percent of participants				
number (not applicable)	5.2	5.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Seronegative Participants Who Achieved an A/H3N2 HAI Antibody Titer ≥ 32 Post Immunogenicity Dose

End point title	Percent of Seronegative Participants Who Achieved an A/H3N2 HAI Antibody Titer ≥ 32 Post Immunogenicity Dose[25]

End point description:

Seronegative was defined as a baseline HAI titer ≤ 4.
All participants who received any investigational product (Q=1385; All FM=927), had post dose HAI antibody measurement at the appropriate time, had no protocol deviation judged to have the potential to interfere with the generation or interpretation of an immune response, and were seronegative to the strain (Q=460; All FM=321).

End point type	Secondary

End point timeframe:

Day 28 post immunogenicity dose

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was related to these respective arms only, hence not reporting statistics for all the arms in the baseline period.

End point values	Q/LAIV (MEDI3250)	All FluMist Group: Seronegative to A/H3N2		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	364	244		
Units: Percent of participants				
number (not applicable)	3.8	4.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Seronegative Participants Who Achieved a B/Yamagata HAI Antibody Titer ≥ 32 Post Immunogenicity Dose

End point title	Percent of Seronegative Participants Who Achieved a B/Yamagata HAI Antibody Titer ≥ 32 Post Immunogenicity Dose[26]

End point description:

Seronegative was defined as a baseline HAI titer ≤ 4.
All participants who received any investigational product (Q=1385; All FM=927), had post dose HAI antibody measurement at the appropriate time, had no protocol deviation judged to have the potential to interfere with the generation or interpretation of an immune response, and were seronegative to the strain (Q=364; All FM=244).

End point type	Secondary

End point timeframe:

Day 28 post immunogenicity dose

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was related to these respective arms only, hence not reporting statistics for all the arms in the baseline period.

End point values	Q/LAIV (MEDI3250)	FluMist/B/Yamagata		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	483	165		
Units: Percent of participants				
number (not applicable)	60.9	70.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Seronegative Participants Who Achieved a B/Victoria HAI Antibody Titer ≥ 32 Post Immunogenicity Dose

End point title	Percent of Seronegative Participants Who Achieved a B/Victoria HAI Antibody Titer ≥ 32 Post Immunogenicity Dose[27]

End point description:

Seronegative was defined as a baseline HAI titer ≤ 4. All participants who received any investigational product (Q=1385; FY=464), had post dose HAI antibody measurement at the appropriate time, had no protocol deviation judged to have the potential to interfere with the generation or interpretation of an immune response, and were seronegative to the strain (Q=487; FV=159).

End point type	Secondary

End point timeframe:

Day 28 post immunogenicity dose

Notes:

[27] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was related to these respective arms only, hence not reporting statistics for all the arms in the baseline period.

End point values	Q/LAIV (MEDI3250)	FluMist/B/Victoria		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	487	159		
Units: Percent of Participants				
number (not applicable)	37	42.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of All Participants Experiencing Each Solicited Symptom From Administration of Investigational Product Through 14 Days Post Dose 1

End point title	Percent of All Participants Experiencing Each Solicited Symptom From Administration of Investigational Product Through 14 Days Post Dose 1[28]

End point description:

Solicited symptoms were fever ≥ 100.4°F (38.0°C), runny/stuffy nose, sore throat, cough, headache, generalized muscle aches, decreased activity level (lethargy) OR tiredness/weakness, decreased appetite. Collection of specific solicited symptoms (sore throat, headache, generalized muscle aches) was omitted when, according to the judgment of the investigator, the subject was too young to reliably report a particular symptom. All participants who received any investigational product (Q=1385; All FM=927) and for whom any follow-up solicited symptom safety data were recorded during the

summarized period (Q=1377; All FM=920).

End point type	Secondary

End point timeframe:

Days 0-14 Post Dose 1

Notes:

[28] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was related to these respective arms only, hence not reporting statistics for all the arms in the baseline period.

End point values	Q/LAIV (MEDI3250)	Post Dose 1 solicited symptoms analyses		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	1377	920		
Units: Percent of Participants				
number (not applicable)				
Any solicited symptom	47.9	47.4		
Fever ≥ 100.4°F (38.0°C)	5.7	3.9		
Fever ≥ 101.3°F (38.5°C)	3.3	2.3		
Fever ≥ 102.2°F (39.0°C)	1.4	0.8		
Fever ≥ 103.1°F (39.5°C)	0.3	0.2		
Fever ≥ 104.0°F (40.0°C)	0.1	0		
Fever ≥ 104.9°F (40.5°C)	0	0		
Runny/stuffy nose	32.3	32		
Sore throat	9.2	10.3		
Cough	15.8	16.8		
Headache	12.5	12.2		
Generalized muscle aches	4.4	4.6		
Decreased activity level or tiredness/weakness	9.8	9.9		
Decreased appetite	5.5	6.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Two-dose Participants Experiencing Each Solicited Symptom From Administration of Investigational Product Through 14 Days Post Dose 1

End point title	Percent of Two-dose Participants Experiencing Each Solicited Symptom From Administration of Investigational Product Through 14 Days Post Dose 1[29]

End point description:

Solicited symptoms were fever ≥ 100.4°F (38.0°C), runny/stuffy nose, sore throat, cough, headache, generalized muscle aches, decreased activity level (lethargy) OR tiredness/weakness, decreased appetite. Collection of specific solicited symptoms (sore throat, headache, generalized muscle aches) was omitted when, according to the judgment of the investigator, the subject was too young to reliably report a particular symptom.
All two-dose participants who received any investigational product (Q=1083; All FM=719) and for whom any follow-up solicited symptom safety data were recorded during the summarized period (Q=1078; All FM=716).

End point type	Secondary

End point timeframe:

Days 0-14 Post Dose 1

Notes:

[29] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was related to these respective arms only, hence not reporting statistics for all the arms in the baseline period.

End point values	Q/LAIV (MEDI3250)	Post-dose 1 solicited symptoms analyses: 2-dose group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	1078	716		
Units: Percent of Participants				
number (not applicable)				
Any solicited symptom	48.1	47.5		
Fever ≥ 100.4°F (38.0°C)	6.6	4.2		
Fever ≥ 101.3°F (38.5°C)	4	2.2		
Fever ≥ 102.2°F (39.0°C)	1.7	0.8		
Fever ≥ 103.1°F (39.5°C)	0.4	0.3		
Fever ≥ 104.0°F (40.0°C)	0.1	0		
Fever ≥ 104.9°F (40.5°C)	0	0		
Runny/stuffy nose	33.8	31.7		
Sore throat	8.2	8.9		
Cough	17.2	18		
Headache	9.7	10.1		
Generalized muscle aches	4.5	4.3		
Decreased activity level or tiredness/weakness	9.3	8.2		
Decreased appetite	5.6	6.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Two-dose Participants Experiencing Each Solicited Symptom From Administration of Dose 2 During Days 0-14 Post Dose 2

End point title	Percent of Two-dose Participants Experiencing Each Solicited Symptom From Administration of Dose 2 During Days 0-14 Post Dose 2[30]

End point description:

Solicited symptoms were fever ≥ 100.4°F (38.0°C), runny/stuffy nose, sore throat, cough, headache, generalized muscle aches, decreased activity level (lethargy) OR tiredness/weakness, decreased appetite. Collection of specific solicited symptoms (sore throat, headache, generalized muscle aches) was omitted when, according to the judgment of the investigator, the subject was too young to reliably report a particular symptom.
All two-dose participants who received any investigational product (Q=1083; All FM=719) and for whom any follow-up solicited symptom safety data were recorded during the summarized period (Q=1039; All FM=692).

End point type	Secondary

End point timeframe:

Days 0-14 Post Dose 2

Notes:

[30] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was related to these respective arms only, hence not reporting statistics for all the arms in the baseline period.

End point values	Q/LAIV (MEDI3250)	Post Dose 2 solicited symptoms analyses		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	1039	692		
Units: Percent of Participants				
number (not applicable)				
Any solicited symptom	31.4	30.6		
Fever ≥ 100.4°F (38.0°C)	2.7	4.2		
Fever ≥ 101.3°F (38.5°C)	1.5	2.3		
Fever ≥ 102.2°F (39.0°C)	0.8	1		
Fever ≥ 103.1°F (39.5°C)	0.3	0.3		
Fever ≥ 104.0°F (40.0°C)	0	0.1		
Fever ≥ 104.9°F (40.5°C)	0	0		
Runny/stuffy nose	20.9	19.5		
Sore throat	4.1	4.6		
Cough	12.7	11.7		
Headache	5.4	5.5		
Generalized muscle aches	1.2	0.9		
Decreased activity level or tiredness/weakness	5.9	5.3		
Decreased appetite	3.7	3.3		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of All Participants Experiencing Any Adverse Event From Administration of Investigational Product Through Day 28 Post Dose 1

End point title	Percent of All Participants Experiencing Any Adverse Event From Administration of Investigational Product Through Day 28 Post Dose 1[31]

End point description:

Any untoward medical occurrence in a patient or clinical investigation in a subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.
All participants who received any investigational product (Q=1385; All FM=927) and for whom any safety data were recorded during the summarized period (Q=1382; All FM=923).

End point type	Secondary

End point timeframe:

Days 0-28 Post Dose 1

Notes:

[31] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was related to these respective arms only, hence not reporting statistics for all the arms in the baseline period.

End point values	Q/LAIV (MEDI3250)	All FluMist Group: Safety population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	1382	923		
Units: Percent of Participants				
number (not applicable)	21	20.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Two-dose Participants Experiencing Any Adverse Event From Administration of Investigational Product Through Day 28 Post Dose 1

End point title	Percent of Two-dose Participants Experiencing Any Adverse Event From Administration of Investigational Product Through Day 28 Post Dose 1[32]

End point description:

Any untoward medical occurrence in a patient or clinical investigation in a subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. All two-dose participants who received any investigational product (Q=1083; All FM=719) and for whom any safety data were recorded during the summarized period (Q=1083; All FM=719).

End point type	Secondary

End point timeframe:

Days 0-28 Post Dose 1

Notes:

[32] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was related to these respective arms only, hence not reporting statistics for all the arms in the baseline period.

End point values	Q/LAIV (MEDI3250)	Safety population: Two-dose group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	1083	719		
Units: Percent of Participants				
number (not applicable)	20.3	22.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Two-dose Participants Experiencing Any Adverse Event From Administration of Dose 2 Through 28 Days Post Dose 2

End point title	Percent of Two-dose Participants Experiencing Any Adverse Event From Administration of Dose 2 Through 28 Days Post Dose 2[33]

End point description:

Any untoward medical occurrence in a patient or clinical investigation in a subject administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.
All two-dose participants who received any investigational product (Q=1083; All FM=719) and for whom any post Dose 2 safety data were recorded during the summariezed period (Q=1041; All FM=693).

End point type	Secondary

End point timeframe:

Days 0-28 Post Dose 2

Notes:

[33] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was related to these respective arms only, hence not reporting statistics for all the arms in the baseline period.

End point values	Q/LAIV (MEDI3250)	Evaluable Safety population: Two-dose group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	1041	693		
Units: Percent of participants				
number (not applicable)	13.4	16.7		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of All Participants Reporting Any Serious Adverse Event (SAE) From Administration of Investigational Product Through Day 28 Post Dose 1

End point title	Percent of All Participants Reporting Any Serious Adverse Event (SAE) From Administration of Investigational Product Through Day 28 Post Dose 1[34]

End point description:

SAEs were those AEs that resulted in death; were immediately life threatening; resulted in inpatient hospitalization or prolongation of existing hospitalization; resulted in persistent or significant disability or incapacity; were a congenital anomaly in the offspring of a participant; or were an important medical event that may not have resulted in death, threatened life, or required hospitalization and that, based on appropriate medical judgement, may have jeopardized the participant and may have required medical or surgical intervention to prevent on the outcomes listed above.
All participants who received any investigational product (Q=1385; All FM=927) and for whom any safety data were recorded during the summarized period (Q=1382; All FM=923).

End point type	Secondary

End point timeframe:

Days 0-28 Post Dose 1

Notes:

[34] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was related to these respective arms only, hence not reporting statistics for all the arms in the baseline period.

End point values	Q/LAIV (MEDI3250)	All FluMist Group: Safety population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	1382	923		
Units: Percent of participants				
number (not applicable)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of Two-dose Participants Reporting Any SAE From Administration of Dose 2 During Days 0-28 Post Dose 2

End point title	Percent of Two-dose Participants Reporting Any SAE From Administration of Dose 2 During Days 0-28 Post Dose 2[35]

End point description:

SAEs were those AEs that resulted in death; were immediately life threatening; resulted in inpatient hospitalization or prolongation of existing hospitalization; resulted in persistent or significant disability or incapacity; were a congenital anomaly in the offspring of a participant; or were an important medical event that may not have resulted in death, threatened life, or required hospitalization and that, based on appropriate medical judgement, may have jeopardized the participant and may have required medical or surgical intervention to prevent on the outcomes listed above.
All two-dose participants who received any investigational product (Q=1083; All FM=719) and for whom any post Dose 2 safety data were recorded during the summarized period (Q=1041; All FM=693).

End point type	Secondary

End point timeframe:

Days 0-28 Post Dose 2

Notes:

[35] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was related to these respective arms only, hence not reporting statistics for all the arms in the baseline period.

End point values	Q/LAIV (MEDI3250)	Evaluable Safety population: Two-dose group		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	1041	693		
Units: Percent of participants				
number (not applicable)	0.2	0.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of All Participants Reporting Any SAE From Administration of Investigational Product Through 180 Days Post Last Dose

End point title	Percent of All Participants Reporting Any SAE From Administration of Investigational Product Through 180 Days Post Last Dose[36]

End point description:

SAEs were those AEs that resulted in death; were immediately life threatening; resulted in inpatient hospitalization or prolongation of existing hospitalization; resulted in persistent or significant disability or incapacity; were a congenital anomaly in the offspring of a participant; or were an important medical event that may not have resulted in death, threatened life, or required hospitalization and that, based on appropriate medical judgement, may have jeopardized the participant and may have required medical or surgical intervention to prevent on the outcomes listed above. All participants who received any investigational product (Q=1385; All FM=927) and for whom any safety data were recorded during the summarized period (Q=1382; All FM=923).

End point type	Secondary

End point timeframe:

Days 0-180 Post Last Dose

Notes:

[36] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was related to these respective arms only, hence not reporting statistics for all the arms in the baseline period.

End point values	Q/LAIV (MEDI3250)	All FluMist Group: Safety population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	1382	923		
Units: Percent of participants				
number (not applicable)	0.4	0.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Percent of All Participants Reporting Any New Onset Chronic Disease

(NOCD) From Administration of Investigational Product Through 180 Days Post Last Dose

End point title	Percent of All Participants Reporting Any New Onset Chronic Disease (NOCD) From Administration of Investigational Product Through 180 Days Post Last Dose[37]

End point description:

An NOCD was a newly diagnosed medical condition that was of a chronic, ongoing nature and was assessed by the investigator as medically significant.
All participants who received any investigational product (Q=1385; All FM=927) and for whom any safety data were recorded during the summarized period (Q=1382; All FM=923).

End point type	Secondary

End point timeframe:

Days 0-180 Post Last Dose

Notes:

[37] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This endpoint was related to these respective arms only, hence not reporting statistics for all the arms in the baseline period.

End point values	Q/LAIV (MEDI3250)	All FluMist Group: Safety population		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	1382	923		
Units: Percent of participants				
number (not applicable)	1.4	0.8		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from Day 0 through 28 after Doses 1 and 2. Serious adverse events were collected between Days 0-180 after the last dose administered.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.0

Reporting groups

Reporting group title	All FluMist Group

Reporting group description:

All FluMist group for A/H1N1 and A/H3N2 strains, where data from both the FluMist/B/Yamagata arm and the FluMist/B/Victoria arm were combined

Reporting group title	Q/LAIV (MEDI3250)

Reporting group description:

Q/LAIV (quadrivalent live attenuated influenza vaccine) (MEDI3250) was supplied in the Becton Dickinson (BD) Accuspray device that delivers a 0.2 mL total volume intranasal dose divided into each nostril (ie, administered as 0.1 mL per nostril). Each 0.2 mL dose contained 10^7.0 ± 0.5 fluorescent focus units (FFU) of each of 4 temperature sensitive, cold-adapted, attenuated, 6:2 resassortant influenza strains (A/H1N1 [A/South Dakota/6/2007], A/H3N2 [A/Uruguay/716/2007], B/Victoria [B/Malaysia/2506/2004], and B/Yamagata [B/Florida/4/2006]).

Serious adverse events	All FluMist Group	Q/LAIV (MEDI3250)	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 923 (0.54%)	6 / 1382 (0.43%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	1 / 923 (0.11%)	0 / 1382 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	0 / 923 (0.00%)	1 / 1382 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung injury			

subjects affected / exposed	1 / 923 (0.11%)	0 / 1382 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 923 (0.11%)	0 / 1382 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumothorax			
subjects affected / exposed	1 / 923 (0.11%)	0 / 1382 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Major depression			
subjects affected / exposed	1 / 923 (0.11%)	0 / 1382 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Pelvi-ureteric obstruction			
subjects affected / exposed	1 / 923 (0.11%)	0 / 1382 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 923 (0.00%)	1 / 1382 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	0 / 923 (0.00%)	1 / 1382 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis salmonella			

subjects affected / exposed	0 / 923 (0.00%)	1 / 1382 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	1 / 923 (0.11%)	0 / 1382 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	2 / 923 (0.22%)	0 / 1382 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 923 (0.00%)	1 / 1382 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	0 / 923 (0.00%)	1 / 1382 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 923 (0.00%)	1 / 1382 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	All FluMist Group	Q/LAIV (MEDI3250)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	105 / 923 (11.38%)	176 / 1382 (12.74%)	
General disorders and administration site conditions			
PYREXIA			

subjects affected / exposed	6 / 923 (0.65%)	23 / 1382 (1.66%)	
occurrences (all)	8	23	
Gastrointestinal disorders			
ABDOMINAL PAIN UPPER			
subjects affected / exposed	12 / 923 (1.30%)	10 / 1382 (0.72%)	
occurrences (all)	14	12	
DIARRHOEA			
subjects affected / exposed	19 / 923 (2.06%)	22 / 1382 (1.59%)	
occurrences (all)	19	22	
VOMITING			
subjects affected / exposed	20 / 923 (2.17%)	36 / 1382 (2.60%)	
occurrences (all)	21	37	
Respiratory, thoracic and mediastinal disorders			
COUGH			
subjects affected / exposed	16 / 923 (1.73%)	27 / 1382 (1.95%)	
occurrences (all)	17	27	
RHINORRHOEA			
subjects affected / exposed	17 / 923 (1.84%)	22 / 1382 (1.59%)	
occurrences (all)	17	23	
SNEEZING			
subjects affected / exposed	8 / 923 (0.87%)	16 / 1382 (1.16%)	
occurrences (all)	10	17	
Infections and infestations			
OTITIS MEDIA			
subjects affected / exposed	12 / 923 (1.30%)	12 / 1382 (0.87%)	
occurrences (all)	12	12	
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	11 / 923 (1.19%)	8 / 1382 (0.58%)	
occurrences (all)	11	8	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 September 2009	Major changes to the study design incorporated in Amendment 1 were: 1) Entire protocol: Remove the blow-fill-seal (BFS) arm; QLAIV was only provided in the BD Accuspray device. This resulted in a change in number of subjects enrolled. The inclusion of the BFS arm did not permit complete blinding of the investigational product due to the differences between the Accuspray and BFS devices. Because the BFS arm was removed, the study was now completely blinded. The protocol title was therefore changed from "A Randomized, Partially Blinded, Active Controlled Study to Evaluate the Immunogenicity of Quadrivalent LAIV in Children" to its current title of "A Randomized, Double-Blind, Active Controlled Study to Evaluate the Immunogenicity of Quadrivalent LAIV in Children" 2) Section 7.3.1 (Primary Endpoint): Amended the statistical analysis section so that the primary endpoint was met if the upper bound of the two-sided 95% CIs for the strainspecific HAI antibody GMT ratios (FluMist divided by Q/LAIV) was ≤ 2 for all 4 strains. 3) Section 7.3.2 (Secondary Endpoints): Amended the definition of seronegative and serosusceptible to include HAI antibody values that were not whole numbers, because each time point was assayed in duplicate, and if the results were within one dilution, the GMT was calculated and used for analysis. Values that differed by more than one dilution for a single specimen were repeated. 4) Section 5.2 (Schedule of Study Procedures): Added a temperature log, which was to be collected. Clarified that a memory aid was supplied to subjects, but it was not considered to be source data and was not collected. 5) Section 1.4.1 (Safety of Q/LAIV in Study MI-CP185): Provided data from on-going Study MI-CP185, a study of Q/LAIV in adults.
09 March 2010	Major changes to the study incorporated in Amendment 2 were: 1) Added unblinded MI-CP185 safety and immunogenicity data. 2) Entire protocol: Clarified that the subject history of prior influenza vaccination that was used to stratify enrollment and to assign the timing of the immunogenicity blood sample was a history of prior seasonal influenza vaccination, because of the possibility that children might have received a prior influenza vaccine that consisted only of monovalent pandemic H1N1. 3) Entire protocol: Amended the noninferiority margin from 2.0 to 1.5 in accordance with guidance from the US FDA. 4) Abstract, Overview of Study Design and Treatment Assignment: Removed site as a stratification factor for randomization, 5) Exclusion Criteria: Modified the concomitant medications window around exclusion criteria numbers 4, 5, 7, 8, 12, 14 from 30 days to 28 days to be consistent with the concomitant medication reporting period and clarified that salicylate-containing medications were prohibited. 6) Exclusion Criteria: Added, "A history of epilepsy, seizure, or an evolving neurological condition except that a single febrile seizure that occurred 3 or more years prior to enrollment would not disqualify a subject" in accordance with guidance from the Canadian IRB. 7) Blinding: Clarified that all MedImmune staff were unblinded for the Day 28 safety and immunogenicity analyses, but site staff, CRO staff, and subjects were to remain blinded until the Day 180 final database lock 8) Concomitant Medications: Modified concomitant medications windows to be consistent with the concomitant medication reporting period and clarified that salicylate-containing medications were prohibited. 9) Clarified the relationship between severity Grading 1-5 and the wording mild, moderate, severe, life-threatening and fatal, because the EDC system contained these words.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported