Clinical trial results:
A Randomized, Double-Blind Trial to Assess the Safety and Relative Efficacy of CAIV-T Against Inactivated Influenza Vaccine in Children 6–59 Months of Age

Summary

EudraCT number	2004-000585-13
Trial protocol	FI SE CZ ES IS GB IT BE
Global end of trial date	31 August 2005

Results information

Result version number	v1 (current)
This version publication date	06 March 2016
First version publication date	06 March 2016

Trial information

Trial identification

Sponsor protocol code	MI-CP111

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00128167
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	MedImmune, LLC
Sponsor organisation address	One MedImmune Way, Gaithersburg, United States, 20878
Public contact	Dr. Raburn Mallory, MedImmune, LLC, +1 301-398-4862,
Scientific contact	Dr. Raburn Mallory, MedImmune, LLC, +1 301-398-4862,

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	31 August 2005
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	31 August 2005
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 estimate the relative efficacy and assess the safety of CAIV-T compared to TIV. It also included to estimate the relative effectiveness of CAIV-T compared to TIV, and to assess the tolerability of CAIV-T compared to TIV.

Protection of trial subjects:

Safety evaluations included adverse events (AEs), serious adverse events (SAEs),concomitant medication use and Reactogenicity event (REs) (which were a subset of solicited events),Significant new medical condition (SNMCs) were also collected.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 October 2004
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 4117
Country: Number of subjects enrolled	Finland: 725
Country: Number of subjects enrolled	Israel: 653
Country: Number of subjects enrolled	United Kingdom: 563
Country: Number of subjects enrolled	Belgium: 459
Country: Number of subjects enrolled	Italy: 316
Country: Number of subjects enrolled	Spain: 238
Country: Number of subjects enrolled	Czech Republic: 139
Country: Number of subjects enrolled	Germany: 109
Country: Number of subjects enrolled	Iceland: 50
Country: Number of subjects enrolled	Hong Kong: 255
Country: Number of subjects enrolled	Taiwan: 178
Country: Number of subjects enrolled	Korea, Republic of: 109
Country: Number of subjects enrolled	Lebanon: 216
Country: Number of subjects enrolled	Sweden: 190
Country: Number of subjects enrolled	Greece: 158
Worldwide total number of subjects	8475
EEA total number of subjects	2947

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)	4024
Children (2-11 years)	4451
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The trial was conducted at 249 sites: 133 sites in the United States, 15 sites in Asia, and 101 sites in Europe/ Middle East. The study was conducted between 20/Oct/04 and 31/Aug/05.

Pre-assignment

Screening details:

A total of 8500 participants were screened; 8475 participants were randomized into the study: 4243 in the CAIV-T group, and 4232 in the TIV group.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Intranasal CAIV-T plus intramuscular placebo

Arm description:

Participants who were previously vaccinated with an influenza vaccine received CAIV-T 0.2 milliliter (mL) once on Day 0 as intranasal spray. Participants who were not vaccinated with and influenza vaccine received CAIV-T 0.2 mL twice as intranasal spray, Dose 1 on Day 0 and dose 2 on Day 28-42 after dose 1. Placebo matching with TIV administered as intramuscular injection along with CAIV-T. CAIV-T contains approximately 10^7 fluorescent focus units (FFU) of each of three cold-adapted, attenuated, reassortant strains representing the hemagglutinin (HA) and neuraminidase (NA) antigens.

Arm type	Experimental
Investigational medicinal product name	Cold-Adapted Influenza Virus Vaccine - Trivalent Liquid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

A total volume of 0.2 mL containing approximately 10t^7 FFU (fluorescent focus units) of each of three cold-adapted, attenuated, reassortant strains representing the hemagglutinin (HA) and neuraminidase (NA) antigens of the influenza strains.

Arm title	Intramuscular TIV plus intranasal placebo

Arm description:

Participants who were previously vaccinated with an influenza vaccine received TIV 0.25 or 0.5 mL once on Day 0 as intranasal spray. Participants who were not vaccinated with and influenza vaccine received TIV 0.25 or 0.5 mL twice as intranasal spray, Dose 1 on Day 0 and Dose 2 on Day 28-42 after dose 1. Placebo matching with CAIV-T administered as intramuscular injection along with TIV. Participant with age of 6-35 months received 0.25 mL and participants with age 36-59 months received 0.5mL of TIV. TIV contains 45 micrograms of Hemagglutinin (HA) per 0.5 mL, in the recommended ratio of 15 micrograms of HA for each of the three influenza strains.

Arm type	Active comparator
Investigational medicinal product name	Vaxigrip
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Nasal use

Dosage and administration details:

A total volume of 0.2 mL containing approximately 10t^7 FFU (fluorescent focus units) of each of three

cold-adapted, attenuated, reassortant strains representing the hemagglutinin (HA) and neuraminidase (NA) antigens of the influenza strains.

Number of subjects in period 1	Intranasal CAIV-T plus intramuscular placebo	Intramuscular TIV plus intranasal placebo
Started	4243	4232
Completed	3933	3911
Not completed	310	321
Consent withdrawn by subject	116	118
Parent/guardian non-compliance	-	1
Subject expired prior to Day 180	1	1
Failed to contact subject's guardian	3	2
Subject moved out of area	2	3
Terminated before Day 180 or 31/05/05	10	17
Subject randomized but never dosed	10	6
Lost to follow-up	168	173

Baseline characteristics

Reporting groups	
Reporting group title	Intranasal CAIV-T plus intramuscular placebo
Reporting group description:	
Participants who were previously vaccinated with an influenza vaccine received CAIV-T 0.2 milliliter (mL) once on Day 0 as intranasal spray. Participants who were not vaccinated with and influenza vaccine received CAIV-T 0.2 mL twice as intranasal spray, Dose 1 on Day 0 and dose 2 on Day 28-42 after dose 1. Placebo matching with TIV administered as intramuscular injection along with CAIV-T. CAIV-T contains approximately 10^7 fluorescent focus units (FFU) of each of three cold-adapted, attenuated, reassortant strains representing the hemagglutinin (HA) and neuraminidase (NA) antigens.	
Reporting group title	Intramuscular TIV plus intranasal placebo
Reporting group description:	
Participants who were previously vaccinated with an influenza vaccine received TIV 0.25 or 0.5 mL once on Day 0 as intranasal spray. Participants who were not vaccinated with and influenza vaccine received TIV 0.25 or 0.5 mL twice as intranasal spray, Dose 1 on Day 0 and Dose 2 on Day 28-42 after dose 1. Placebo matching with CAIV-T administered as intramuscular injection along with TIV. Participant with age of 6-35 months received 0.25 mL and participants with age 36-59 months received 0.5mL of TIV. TIV contains 45 micrograms of Hemagglutinin (HA) per 0.5 mL, in the recommended ratio of 15 micrograms of HA for each of the three influenza strains.	

Reporting group values	Intranasal CAIV-T plus intramuscular placebo	Intramuscular TIV plus intranasal placebo	Total
Number of subjects	4243	4232	8475
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			0
Newborns (0-27 days)			0
Infants and toddlers (28 days-23 months)			0
Children (2-11 years)			0
Adolescents (12-17 years)			0
Adults (18-64 years)			0
From 65-84 years			0
85 years and over			0
Age Continuous | Units: months			
arithmetic mean	25.7	25.6	
standard deviation	± 13.4	± 13.2	-
Gender, Male/Female Units: participants			
Female	2065	2055	4120
Male	2178	2177	4355

End points

End points reporting groups

Reporting group title	Intranasal CAIV-T plus intramuscular placebo

Reporting group description:

Participants who were previously vaccinated with an influenza vaccine received CAIV-T 0.2 milliliter (mL) once on Day 0 as intranasal spray. Participants who were not vaccinated with and influenza vaccine received CAIV-T 0.2 mL twice as intranasal spray, Dose 1 on Day 0 and dose 2 on Day 28-42 after dose 1. Placebo matching with TIV administered as intramuscular injection along with CAIV-T. CAIV-T contains approximately 10^7 fluorescent focus units (FFU) of each of three cold-adapted, attenuated, reassortant strains representing the hemagglutinin (HA) and neuraminidase (NA) antigens.

Reporting group title	Intramuscular TIV plus intranasal placebo

Reporting group description:

Participants who were previously vaccinated with an influenza vaccine received TIV 0.25 or 0.5 mL once on Day 0 as intranasal spray. Participants who were not vaccinated with and influenza vaccine received TIV 0.25 or 0.5 mL twice as intranasal spray, Dose 1 on Day 0 and Dose 2 on Day 28-42 after dose 1. Placebo matching with CAIV-T administered as intramuscular injection along with TIV. Participant with age of 6-35 months received 0.25 mL and participants with age 36-59 months received 0.5mL of TIV. TIV contains 45 micrograms of Hemagglutinin (HA) per 0.5 mL, in the recommended ratio of 15 micrograms of HA for each of the three influenza strains.

Subject analysis set title	One Dose Group (CAIV-T)
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants receive a single dose of study vaccine plus corresponding placebo (Dose One) on Study Day 0.

Subject analysis set title	One Dose Group (TIV)
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants receive a single dose of study vaccine plus corresponding placebo (Dose One) on Study Day 0.

Subject analysis set title	Two dose Group (CAIV-T) - After Dose 1
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants who never previously received an influenza vaccination (or had an unknown history of influenza vaccination) were to receive two doses of study vaccine plus corresponding placebo: Dose One on Study Day 0 and Dose Two 28-42 days after the first dose.

Subject analysis set title	Two Dose Group (TIV) - After Dose 1
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants who never previously received an influenza vaccination (or had an unknown history of influenza vaccination) were to receive two doses of study vaccine plus corresponding placebo: Dose One on Study Day 0 and Dose Two 28-42 days after the first dose.

Subject analysis set title	Two dose Group (CAIV-T) - After Dose 2
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants who never previously received an influenza vaccination (or had an unknown history of influenza vaccination) were to receive two doses of study vaccine plus corresponding placebo: Dose One on Study Day 0 and Dose Two 28-42 days after the first dose.

Subject analysis set title	Two dose Group (TIV) - After Dose 2
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants who never previously received an influenza vaccination (or had an unknown history of influenza vaccination) were to receive two doses of study vaccine plus corresponding placebo: Dose One on Study Day 0 and Dose Two 28-42 days after the first dose.

Subject analysis set title	One Dose Group (CAIV-T)
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants receive a single dose of study vaccine plus corresponding placebo (Dose One) on Study Day 0.

Subject analysis set title	One Dose Group (TIV)
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants receive a single dose of study vaccine plus corresponding placebo (Dose One) on Study Day 0.

Subject analysis set title	Two dose Group (CAIV-T) - After Dose 1
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants who never previously received an influenza vaccination (or had an unknown history of influenza vaccination) were to receive two doses of study vaccine plus corresponding placebo: Dose One on Study Day 0 and Dose Two 28-42 days after the first dose.

Subject analysis set title	Two Dose Group (TIV) - After Dose 1
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants who never previously received an influenza vaccination (or had an unknown history of influenza vaccination) were to receive two doses of study vaccine plus corresponding placebo: Dose One on Study Day 0 and Dose Two 28-42 days after the first dose.

Subject analysis set title	Two dose Group (CAIV-T) - After Dose 2
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants who never previously received an influenza vaccination (or had an unknown history of influenza vaccination) were to receive two doses of study vaccine plus corresponding placebo: Dose One on Study Day 0 and Dose Two 28-42 days after the first dose.

Subject analysis set title	Two dose Group (TIV) - After Dose 2
Subject analysis set type	Safety analysis

Subject analysis set description:

Participants who never previously received an influenza vaccination (or had an unknown history of influenza vaccination) were to receive two doses of study vaccine plus corresponding placebo: Dose One on Study Day 0 and Dose Two 28-42 days after the first dose.

Primary: Number of Participants With Culture-Confirmed Modified Influenza-Like-Illness per the Centers for Disease Control (CDC-ILI) Caused by Wild-Type Strains

End point title	Number of Participants With Culture-Confirmed Modified Influenza-Like-Illness per the Centers for Disease Control (CDC-ILI) Caused by Wild-Type Strains

End point description:

The CDC-ILI (CDC-defined influenza-like illness), defined as fever (temperature >=100°F oral or equivalent) plus cough or sore throat on the same or consecutive days, was modified ("modified CDC-ILI") to fever plus cough, sore throat, or runny nose/nasal congestion as a means of capturing age-appropriate influenza illness symptoms. Modified CDC-ILI was defined as a positive culture for a wild-type influenza virus associated within >=7 days of modified CDC-ILI symptoms.

End point type	Primary

End point timeframe:

14 days after last dose of study vaccination

End point values	Intranasal CAIV-T plus intramuscular placebo	Intramuscular TIV plus intranasal placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4243	4232		
Units: participants				
Antigenically Similar: All strains	53	93		
Antigenically Dissimilar: All strains	102	245		
Regardless of Antigenic Match: All strains	153	338		

Statistical analyses

Statistical analysis title	Relative efficacy - Antigenically Similar
Statistical analysis description:	
Antigenically Similar: All strains - relative efficacy was adjusted for country, age, prior vaccination status, and wheezing history status.	
Comparison groups	Intramuscular TIV plus intranasal placebo v Intranasal CAIV-T plus intramuscular placebo
Number of subjects included in analysis	8475
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted Relative efficacy
Point estimate	44.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	22.4
upper limit	60.6

Statistical analysis title	Relative Efficacy - Antigenically Dissimilar
Statistical analysis description:	
Antigenically Dissimilar: All strains - relative efficacy was adjusted for country, age, prior vaccination status, and wheezing history status.	
Comparison groups	Intranasal CAIV-T plus intramuscular placebo v Intramuscular TIV plus intranasal placebo
Number of subjects included in analysis	8475
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted Relative efficacy
Point estimate	58.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	47
upper limit	67

Statistical analysis title	Relative efficacy - Regardless of Antigenic Match
Statistical analysis description:	
Regardless of Antigenic Match: All strains - relative efficacy was adjusted for country, age, prior vaccination status, and wheezing history status.	
Comparison groups	Intranasal CAIV-T plus intramuscular placebo v Intramuscular TIV plus intranasal placebo
Number of subjects included in analysis	8475
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted Relative efficacy
Point estimate	54.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	45.4
upper limit	62.9

Secondary: Number of Participants With Culture-confirmed Symptomatic Influenza Infection Caused by Wild-type Strains

End point title	Number of Participants With Culture-confirmed Symptomatic Influenza Infection Caused by Wild-type Strains
End point description:	
Culture-confirmed symptomatic influenza infection was defined as a positive culture for a community-acquired wild-type influenza virus associated within 7 days with one (or more) of the qualifying illness symptoms: fever (temperature 99.8°F oral or equivalent), wheezing, shortness of breath, pulmonary congestion (including bronchitis, bronchiolitis, and croup), pneumonia, or ear infection (acute otitis media, suspected or diagnosed); OR at least two of the following symptoms concurrently: runny/stuffy nose (rhinorrhea), sore throat (pharyngitis), cough, muscle aches, chills, headache, irritability, decreased activity, or vomiting.	
End point type	Secondary
End point timeframe:	
14 days after last dose of study vaccination	

End point values	Intranasal CAIV-T plus intramuscular placebo	Intramuscular TIV plus intranasal placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3916	3936		
Units: participants				
Antigenically Similar: All strains	22	33		
Antigenically Dissimilar: All strains	31	98		
Regardless of Antigenic Match: All strains	0	0		

Statistical analyses

Statistical analysis title	Relative efficacy - Antigenically Similar
Statistical analysis description:	
Antigenically Similar: All strains - relative efficacy was adjusted for country, age, prior vaccination status, and wheezing history status.	
Comparison groups	Intranasal CAIV-T plus intramuscular placebo v Intramuscular TIV plus intranasal placebo
Number of subjects included in analysis	7852
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted Relative efficacy
Point estimate	34.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.2
upper limit	62.4

Statistical analysis title	Relative efficacy - Antigenically Dissimilar
Statistical analysis description:	
Antigenically Dissimilar: All strains - relative efficacy was adjusted for country, age, prior vaccination status, and wheezing history status.	
Comparison groups	Intranasal CAIV-T plus intramuscular placebo v Intramuscular TIV plus intranasal placebo
Number of subjects included in analysis	7852
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted Relative efficacy
Point estimate	68.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	53.1
upper limit	79.2

Statistical analysis title	Relative efficacy - Regardless of Antigenic Match
Statistical analysis description:	
Regardless of Antigenic Match: All strains - relative efficacy was adjusted for country, age, prior vaccination status, and wheezing history status.	
Comparison groups	Intranasal CAIV-T plus intramuscular placebo v Intramuscular TIV plus intranasal placebo

Number of subjects included in analysis	7852
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Adjusted Relative efficacy
Point estimate	62.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	48.1
upper limit	73

Secondary: Number of Participants With Reactogenicity Events

End point title	Number of Participants With Reactogenicity Events

End point description:

Reactogenicity events included Runny/stuffy nose. sore throat, cough, vomiting, headache, muscle ache, chills, decreased activity, irritability, abdominal pain, decreased appetite and fever 100 - 104 degree Fahrenheit.

End point type	Secondary

End point timeframe:

Day 0 to 10

End point values	One Dose Group (CAIV-T)	One Dose Group (TIV)	Two dose Group (CAIV-T) - After Dose 1	Two Dose Group (TIV) - After Dose 1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	933	947	3246	3226
Units: Participants	641	597	2232	1998

End point values	Two dose Group (CAIV-T) - After Dose 2	Two dose Group (TIV) - After Dose 2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	3002	3034		
Units: Participants	1633	1537		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Injection Site Reactions

End point title	Number of Participants With Injection Site Reactions

End point description:

Injection site reactions included injection site pain, injection site redness and injection site swelling.

End point type	Secondary

End point timeframe:

Day 0 to 10

End point values	One Dose Group (CAIV-T)	One Dose Group (TIV)	Two dose Group (CAIV-T) - After Dose 1	Two Dose Group (TIV) - After Dose 1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	929	935	3205	3179
Units: Participants	266	340	677	788

End point values	Two dose Group (CAIV-T) - After Dose 2	Two dose Group (TIV) - After Dose 2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2997	3001		
Units: Participants	439	596		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Reporting Treatment-Emergent Adverse Events (TEAEs) and Treatment-Emergent Serious Adverse Events (TESAEs)

End point title	Number of Participants Reporting Treatment-Emergent Adverse Events (TEAEs) and Treatment-Emergent Serious Adverse Events (TESAEs)

End point description:

An adverse event (AE) was any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. A serious adverse event (SAE) was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Treatment-emergent are events between administration of study drug and up to Day 180 that were absent before treatment or that worsened relative to pre-treatment state. TEAEs reported below included both SAEs and non-serious AEs.

End point type	Secondary

End point timeframe:

Day 0 to 180

End point values	One Dose Group (CAIV-T)	One Dose Group (TIV)	Two dose Group (CAIV-T) - After Dose 1	Two Dose Group (TIV) - After Dose 1
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	933	947	3246	3226
Units: Participants				
TEAEs	311	301	1105	1109
TESAEs	3	7	22	16

End point values	Two dose Group (CAIV-T) - After Dose 2	Two dose Group (TIV) - After Dose 2		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	3002	3034		
Units: Participants				
TEAEs	813	824		
TESAEs	22	25		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants with Medically Significant Wheezing

End point title	Number of Participants with Medically Significant Wheezing

End point description:

Post hoc analyses were performed to evaluate whether subjects who experienced medically significant wheezing were more likely to be subsequently diagnosed with a new condition of asthma, bronchospasm, or wheezing.

End point type	Secondary

End point timeframe:

Upto 42 days post last dose

End point values	Intranasal CAIV-T plus intramuscular placebo	Intramuscular TIV plus intranasal placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4179	4173		
Units: Participants				
Participants: Medically Significant Wheezing	164	131		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 0 to 180 post last dose

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	8.0

Reporting groups

Reporting group title	Intranasal CAIV-T plus intramuscular placebo

Reporting group description:

Participants who were previously vaccinated with an influenza vaccine received CAIV-T 0.2 milliliter (mL) once on Day 0 as intranasal spray. Participants who were not vaccinated with and influenza vaccine received CAIV-T 0.2 mL twice as intranasal spray, Dose one on Day 0 and dose 2 on Day 28-42 days after dose 1. Placebo matching with TIV administered as intramuscular injection along with CAIV-T. CAIV-T contains g approximately 10^7 fluorescent focus units (FFU) of each of three cold-adapted, attenuated, reassortant strains representing the hemagglutinin (HA) and neuraminidase (NA) antigens of the following influenza strains.

Reporting group title	TOTAL

Reporting group description: -

Reporting group title	Intramuscular TIV plus intranasal placebo

Reporting group description:

Participants who were previously vaccinated with an influenza vaccine received TIV 0.25 or 0.5 mL once on Day 0 as intranasal spray. Participants who were not vaccinated with and influenza vaccine received TIV 0.25 or 0.5 mL twice as intranasal spray, Dose one on Day 0 and Dose 2 on Day 28-42 days after dose 1. Placebo matching with CAIV-T administered as intramuscular injection along with TIV. Participant with age of 6-35 months received 0.25 mL and participants with age 6-35 mL received 0.5mL of TIV. TIV contains 45 micrograms of Hemagglutinin (HA) per 0.5 mL, in the recommended ratio of 15 micrograms of HA for each of the three influenza strains.

Serious adverse events	Intranasal CAIV-T plus intramuscular placebo	TOTAL	Intramuscular TIV plus intranasal placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	140 / 4179 (3.35%)	272 / 8351 (3.26%)	132 / 4172 (3.16%)
number of deaths (all causes)	2	2	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute lymphocytic leukaemia			
subjects affected / exposed	1 / 4179 (0.02%)	1 / 8351 (0.01%)	0 / 4172 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myeloid leukaemia			

subjects affected / exposed	1 / 4179 (0.02%)	1 / 8351 (0.01%)	0 / 4172 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuroblastoma			
subjects affected / exposed	1 / 4179 (0.02%)	1 / 8351 (0.01%)	0 / 4172 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Blood stem cell harvest			
subjects affected / exposed	1 / 4179 (0.02%)	1 / 8351 (0.01%)	0 / 4172 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Accidental death			
subjects affected / exposed	0 / 4179 (0.00%)	1 / 8351 (0.01%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Catheter related complication			
subjects affected / exposed	1 / 4179 (0.02%)	1 / 8351 (0.01%)	0 / 4172 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	1 / 4179 (0.02%)	2 / 8351 (0.02%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Drug hypersensitivity			
subjects affected / exposed	1 / 4179 (0.02%)	1 / 8351 (0.01%)	0 / 4172 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Adenoidal disorder			

subjects affected / exposed	1 / 4179 (0.02%)	2 / 8351 (0.02%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	1 / 4179 (0.02%)	1 / 8351 (0.01%)	0 / 4172 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchospasm			
subjects affected / exposed	3 / 4179 (0.07%)	6 / 8351 (0.07%)	3 / 4172 (0.07%)
occurrences causally related to treatment / all	1 / 4	1 / 7	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary congestion			
subjects affected / exposed	0 / 4179 (0.00%)	1 / 8351 (0.01%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillar hypertrophy			
subjects affected / exposed	3 / 4179 (0.07%)	4 / 8351 (0.05%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 3	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wheezing			
subjects affected / exposed	3 / 4179 (0.07%)	5 / 8351 (0.06%)	2 / 4172 (0.05%)
occurrences causally related to treatment / all	1 / 4	2 / 6	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
White blood cell count increased			
subjects affected / exposed	1 / 4179 (0.02%)	1 / 8351 (0.01%)	0 / 4172 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Accidental exposure			
subjects affected / exposed	0 / 4179 (0.00%)	3 / 8351 (0.04%)	3 / 4172 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Animal bite			
subjects affected / exposed	0 / 4179 (0.00%)	1 / 8351 (0.01%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone fissure			
subjects affected / exposed	1 / 4179 (0.02%)	1 / 8351 (0.01%)	0 / 4172 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	1 / 4179 (0.02%)	3 / 8351 (0.04%)	2 / 4172 (0.05%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electric shock			
subjects affected / exposed	1 / 4179 (0.02%)	1 / 8351 (0.01%)	0 / 4172 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Forearm fracture			
subjects affected / exposed	0 / 4179 (0.00%)	2 / 8351 (0.02%)	2 / 4172 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
subjects affected / exposed	1 / 4179 (0.02%)	3 / 8351 (0.04%)	2 / 4172 (0.05%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	0 / 4179 (0.00%)	1 / 8351 (0.01%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury			
subjects affected / exposed	1 / 4179 (0.02%)	1 / 8351 (0.01%)	0 / 4172 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury asphyxiation			

subjects affected / exposed	1 / 4179 (0.02%)	1 / 8351 (0.01%)	0 / 4172 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Jaw fracture			
subjects affected / exposed	0 / 4179 (0.00%)	1 / 8351 (0.01%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thermal burn			
subjects affected / exposed	3 / 4179 (0.07%)	4 / 8351 (0.05%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 3	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Atrioventricular septal defect			
subjects affected / exposed	1 / 4179 (0.02%)	1 / 8351 (0.01%)	0 / 4172 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Autism			
subjects affected / exposed	0 / 4179 (0.00%)	1 / 8351 (0.01%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Convulsion			
subjects affected / exposed	3 / 4179 (0.07%)	3 / 8351 (0.04%)	0 / 4172 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 4179 (0.00%)	1 / 8351 (0.01%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile convulsion			
subjects affected / exposed	5 / 4179 (0.12%)	14 / 8351 (0.17%)	9 / 4172 (0.22%)
occurrences causally related to treatment / all	0 / 5	2 / 15	2 / 10
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Hydrocephalus			
subjects affected / exposed	0 / 4179 (0.00%)	1 / 8351 (0.01%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post-traumatic epilepsy			
subjects affected / exposed	0 / 4179 (0.00%)	1 / 8351 (0.01%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Leukocytosis			
subjects affected / exposed	1 / 4179 (0.02%)	1 / 8351 (0.01%)	0 / 4172 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphadenitis			
subjects affected / exposed	1 / 4179 (0.02%)	1 / 8351 (0.01%)	0 / 4172 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	1 / 4179 (0.02%)	1 / 8351 (0.01%)	0 / 4172 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 4179 (0.05%)	2 / 8351 (0.02%)	0 / 4172 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis perforated			
subjects affected / exposed	0 / 4179 (0.00%)	1 / 8351 (0.01%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 4179 (0.00%)	3 / 8351 (0.04%)	3 / 4172 (0.07%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Enterocolitis			
subjects affected / exposed	0 / 4179 (0.00%)	1 / 8351 (0.01%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	3 / 4179 (0.07%)	4 / 8351 (0.05%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 3	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	1 / 4179 (0.02%)	1 / 8351 (0.01%)	0 / 4172 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Erythema multiforme			
subjects affected / exposed	0 / 4179 (0.00%)	1 / 8351 (0.01%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Henoch-schonlein purpura			
subjects affected / exposed	1 / 4179 (0.02%)	2 / 8351 (0.02%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
subjects affected / exposed	0 / 4179 (0.00%)	1 / 8351 (0.01%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria generalised			
subjects affected / exposed	0 / 4179 (0.00%)	1 / 8351 (0.01%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Anuria			
subjects affected / exposed	1 / 4179 (0.02%)	1 / 8351 (0.01%)	0 / 4172 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 4179 (0.02%)	1 / 8351 (0.01%)	0 / 4172 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Acute sinusitis			
subjects affected / exposed	0 / 4179 (0.00%)	1 / 8351 (0.01%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute tonsillitis			
subjects affected / exposed	1 / 4179 (0.02%)	2 / 8351 (0.02%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenovirus infection			
subjects affected / exposed	0 / 4179 (0.00%)	1 / 8351 (0.01%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	0 / 4179 (0.00%)	2 / 8351 (0.02%)	2 / 4172 (0.05%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis			
subjects affected / exposed	7 / 4179 (0.17%)	13 / 8351 (0.16%)	6 / 4172 (0.14%)
occurrences causally related to treatment / all	2 / 7	2 / 13	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	5 / 4179 (0.12%)	5 / 8351 (0.06%)	0 / 4172 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchopneumonia			
subjects affected / exposed	1 / 4179 (0.02%)	2 / 8351 (0.02%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Croup infectious			
subjects affected / exposed	1 / 4179 (0.02%)	6 / 8351 (0.07%)	5 / 4172 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 6	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Exanthema subitum			
subjects affected / exposed	0 / 4179 (0.00%)	1 / 8351 (0.01%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	21 / 4179 (0.50%)	44 / 8351 (0.53%)	23 / 4172 (0.55%)
occurrences causally related to treatment / all	1 / 22	1 / 45	0 / 23
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis rotavirus			
subjects affected / exposed	5 / 4179 (0.12%)	12 / 8351 (0.14%)	7 / 4172 (0.17%)
occurrences causally related to treatment / all	0 / 5	0 / 12	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis salmonella			
subjects affected / exposed	0 / 4179 (0.00%)	1 / 8351 (0.01%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	3 / 4179 (0.07%)	5 / 8351 (0.06%)	2 / 4172 (0.05%)
occurrences causally related to treatment / all	0 / 3	1 / 5	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Giardiasis			
subjects affected / exposed	0 / 4179 (0.00%)	1 / 8351 (0.01%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hand-foot-and-mouth disease			
subjects affected / exposed	0 / 4179 (0.00%)	1 / 8351 (0.01%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpangina			

subjects affected / exposed	1 / 4179 (0.02%)	2 / 8351 (0.02%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpetic gingivostomatitis			
subjects affected / exposed	3 / 4179 (0.07%)	4 / 8351 (0.05%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 3	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpetic stomatitis			
subjects affected / exposed	1 / 4179 (0.02%)	1 / 8351 (0.01%)	0 / 4172 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 4179 (0.00%)	1 / 8351 (0.01%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngitis			
subjects affected / exposed	1 / 4179 (0.02%)	3 / 8351 (0.04%)	2 / 4172 (0.05%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymph node abscess			
subjects affected / exposed	1 / 4179 (0.02%)	1 / 8351 (0.01%)	0 / 4172 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mastoiditis			
subjects affected / exposed	1 / 4179 (0.02%)	1 / 8351 (0.01%)	0 / 4172 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	2 / 4179 (0.05%)	2 / 8351 (0.02%)	0 / 4172 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis externa			

subjects affected / exposed	0 / 4179 (0.00%)	1 / 8351 (0.01%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media acute			
subjects affected / exposed	3 / 4179 (0.07%)	6 / 8351 (0.07%)	3 / 4172 (0.07%)
occurrences causally related to treatment / all	0 / 3	0 / 6	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Periorbital cellulitis			
subjects affected / exposed	3 / 4179 (0.07%)	4 / 8351 (0.05%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 3	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis			
subjects affected / exposed	1 / 4179 (0.02%)	1 / 8351 (0.01%)	0 / 4172 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngitis streptococcal			
subjects affected / exposed	1 / 4179 (0.02%)	2 / 8351 (0.02%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngotonsillitis			
subjects affected / exposed	2 / 4179 (0.05%)	2 / 8351 (0.02%)	0 / 4172 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	31 / 4179 (0.74%)	57 / 8351 (0.68%)	26 / 4172 (0.62%)
occurrences causally related to treatment / all	0 / 32	0 / 60	0 / 28
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia respiratory syncytial viral			
subjects affected / exposed	1 / 4179 (0.02%)	1 / 8351 (0.01%)	0 / 4172 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			

subjects affected / exposed	1 / 4179 (0.02%)	2 / 8351 (0.02%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	3 / 4179 (0.07%)	3 / 8351 (0.04%)	0 / 4172 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	1 / 4179 (0.02%)	1 / 8351 (0.01%)	0 / 4172 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin bacterial infection			
subjects affected / exposed	1 / 4179 (0.02%)	1 / 8351 (0.01%)	0 / 4172 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Streptococcal infection			
subjects affected / exposed	1 / 4179 (0.02%)	1 / 8351 (0.01%)	0 / 4172 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	1 / 4179 (0.02%)	1 / 8351 (0.01%)	0 / 4172 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	1 / 4179 (0.02%)	1 / 8351 (0.01%)	0 / 4172 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	6 / 4179 (0.14%)	14 / 8351 (0.17%)	8 / 4172 (0.19%)
occurrences causally related to treatment / all	0 / 6	0 / 15	0 / 9
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			

subjects affected / exposed	1 / 4179 (0.02%)	2 / 8351 (0.02%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	2 / 4179 (0.05%)	3 / 8351 (0.04%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 4179 (0.00%)	1 / 8351 (0.01%)	1 / 4172 (0.02%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 4179 (0.02%)	5 / 8351 (0.06%)	4 / 4172 (0.10%)
occurrences causally related to treatment / all	0 / 1	0 / 5	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	1 / 4179 (0.02%)	1 / 8351 (0.01%)	0 / 4172 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Intranasal CAIV-T plus intramuscular placebo	TOTAL	Intramuscular TIV plus intranasal placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2708 / 4179 (64.80%)	5372 / 8351 (64.33%)	2664 / 4172 (63.85%)
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	40 / 4179 (0.96%)	80 / 8351 (0.96%)	40 / 4172 (0.96%)
occurrences (all)	42	84	42
Eye disorders			
Conjunctivitis			
subjects affected / exposed	146 / 4179 (3.49%)	306 / 8351 (3.66%)	160 / 4172 (3.84%)
occurrences (all)	156	326	170

Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	464 / 4179 (11.10%)	937 / 8351 (11.22%)	473 / 4172 (11.34%)
occurrences (all)	610	1236	626
Teething			
subjects affected / exposed	238 / 4179 (5.70%)	493 / 8351 (5.90%)	255 / 4172 (6.11%)
occurrences (all)	355	732	377
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	65 / 4179 (1.56%)	123 / 8351 (1.47%)	58 / 4172 (1.39%)
occurrences (all)	74	145	71
Dyspnoea			
subjects affected / exposed	81 / 4179 (1.94%)	171 / 8351 (2.05%)	90 / 4172 (2.16%)
occurrences (all)	100	218	118
Pulmonary congestion			
subjects affected / exposed	105 / 4179 (2.51%)	199 / 8351 (2.38%)	94 / 4172 (2.25%)
occurrences (all)	142	256	114
Sneezing			
subjects affected / exposed	52 / 4179 (1.24%)	96 / 8351 (1.15%)	44 / 4172 (1.05%)
occurrences (all)	77	135	58
Wheezing			
subjects affected / exposed	463 / 4179 (11.08%)	898 / 8351 (10.75%)	435 / 4172 (10.43%)
occurrences (all)	657	1295	638
Skin and subcutaneous tissue disorders			
Dermatitis diaper			
subjects affected / exposed	62 / 4179 (1.48%)	130 / 8351 (1.56%)	68 / 4172 (1.63%)
occurrences (all)	78	161	83
Rash			
subjects affected / exposed	97 / 4179 (2.32%)	234 / 8351 (2.80%)	137 / 4172 (3.28%)
occurrences (all)	106	254	148
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	115 / 4179 (2.75%)	231 / 8351 (2.77%)	116 / 4172 (2.78%)
occurrences (all)	135	265	130
Croup infectious			

subjects affected / exposed	221 / 4179 (5.29%)	442 / 8351 (5.29%)	221 / 4172 (5.30%)
occurrences (all)	261	521	260
Bronchitis			
subjects affected / exposed	369 / 4179 (8.83%)	721 / 8351 (8.63%)	352 / 4172 (8.44%)
occurrences (all)	447	875	428
Gastroenteritis			
subjects affected / exposed	74 / 4179 (1.77%)	147 / 8351 (1.76%)	73 / 4172 (1.75%)
occurrences (all)	76	150	74
Otitis media acute			
subjects affected / exposed	1431 / 4179 (34.24%)	2858 / 8351 (34.22%)	1427 / 4172 (34.20%)
occurrences (all)	2316	4709	2393
Pharyngitis			
subjects affected / exposed	36 / 4179 (0.86%)	81 / 8351 (0.97%)	45 / 4172 (1.08%)
occurrences (all)	37	83	46
Sinusitis			
subjects affected / exposed	69 / 4179 (1.65%)	128 / 8351 (1.53%)	59 / 4172 (1.41%)
occurrences (all)	74	137	63
Pneumonia			
subjects affected / exposed	131 / 4179 (3.13%)	267 / 8351 (3.20%)	136 / 4172 (3.26%)
occurrences (all)	138	285	147

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 June 2004	Similarily Version 2.0 of the protocol was amended to Version 3.0. The major changes included: increased sample size and corresponding power calculations; clarified the upper age limit for eligibility; clarified criteria for temperature recording; added conditions for dose administration; indicated that study vaccine blinding, supplies, and dispensing at Asian sites would be similar to those of U.S. sites, and that a dedicated SPA would be used in the U.S. and Asia for consistency with European/Middle Eastern countries (where dedicated SPAs were already in use due to the unavailability of blinded study vaccine at these sites); added more details on primary end points and definition of Local respiratory infection (LRI); Revised the evaluation of the confidence intervals, non-inferiority prior to superiority, consistency with the principles of "closed tests."
23 July 2004	In study MI-CP111, Version 1.0 of the protocol was amended to Version 2.0 which included the following changes: increase in number of sites needed for subject recruitment and excluded children with a history of severe asthma.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported