



## Clinical trial results:

### A Phase 3 Randomized, Double-blind Study to Evaluate the Efficacy and Safety of MEDI3250 Compared to Placebo in Healthy Japanese Children age 7 years through 18 years

#### Summary

EudraCT number	2014-003400-70
Trial protocol	Outside EU/EEA
Global end of trial date	20 October 2015

#### Results information

Result version number	v1
This version publication date	20 March 2016
First version publication date	20 March 2016

#### Trial information

##### Trial identification

Sponsor protocol code	D2560C00006
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##### Additional study identifiers

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

Notes:

#### Sponsors

Sponsor organisation name	AstraZeneca Clinical Study Information Center
Sponsor organisation address	Room Tatnall Bldg 1800 Concord Pike PO Box 15437, Wilmington, DE, United States, 19850-5437
Public contact	INformation Center, AstraZeneca Clinical Study Information Center, 1+ 877-240-9479, informationcenter@astrazeneca.com
Scientific contact	Raburn Mallony, MedImmune, 1+ 301-398-0000, ClinicalTrialEnquiries@Medimmune.com

Notes:

#### Paediatric regulatory details

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

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 October 2015
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	20 October 2015
Was the trial ended prematurely?	Yes

Notes:

## General information about the trial

Main objective of the trial:

To assess the efficacy (the incidence of laboratory-confirmed influenza infection caused by any community-acquired wild-type strains matched to the vaccine) of MEDI3250 compared to placebo.

To assess the safety and tolerability of MEDI3250 compared to placebo.

Protection of trial subjects:

The study will be performed in accordance with ethical principles that have their origin in the Declaration of Helsinki and are consistent with ICH/Good Clinical Practice, applicable regulatory requirements and the AstraZeneca policy on Bioethics and Human Biological Samples.

The applicable regulatory requirements in Japan are 'Good Clinical Practice for Trials on Drugs (MHLW Ordinance No. 28, 27 March 1997, partially revised by MHLW Ordinance and their related notifications.

The Master Informed Consent Form will explain that:

- Study data will be stored in a computer database, maintaining confidentiality in accordance with national data legislation
- Subject data will be maintaining confidentiality in accordance with national data legislation
- For data verification purposes, authorised representatives of AstraZeneca, a regulatory authority, an IRB may require direct access to parts of the hospital or practice source records relevant to the study, including subjects' medical history
- All data computer processed by AstraZeneca will be identified by study code and enrolment code (E-code)

The combined data from the trivalent live, attenuated influenza vaccine development program and postmarketing experience provide substantial evidence to confirm the acceptable safety, tolerability, and efficacy of T/LAIV in individuals 24 months of age and older.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 October 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Japan: 1369
Worldwide total number of subjects	1369
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)	849
Adolescents (12-17 years)	486
Adults (18-64 years)	34
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

To enrol Japanese children age 7 years to through 18 years.

### Pre-assignment

Screening details:

To meet all of the inclusion criteria and none of the exclusion criteria for this study.

### Pre-assignment period milestones

Number of subjects started	1369
Number of subjects completed	1301

### Pre-assignment subject non-completion reasons

Reason: Number of subjects	last patients randomization: 68
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### Period 1

Period 1 title	Up to end April 2015 (6 months) (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	MEDI3250

Arm description: -

Arm type	Experimental
Investigational medicinal product name	N/A
Investigational medicinal product code	MEDI3250
Other name	
Pharmaceutical forms	Suspension and solution for spray
Routes of administration	Nasal use

Dosage and administration details:

intranasal administration of 0.2 mL (0.1 mL per nostril)

<b>Arm title</b>	Placebo
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Arm description: -

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

Dosage and administration details:

intranasal administration of 0.2 mL (0.1 mL per nostril)

<b>Number of subjects in period 1<sup>[1]</sup></b>	MEDI3250	Placebo
Started	868	433
Completed	865	432
Not completed	3	1
Consent withdrawn by subject	-	1
exclusion criteria 17	3	-

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Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: A total of 1,369 Japanese subjects whom written informed consent was provided were enrolled. Of these, 1,301 subjects were randomized to either MEDI3250 or placebo and received the investigational product.

## Baseline characteristics

### Reporting groups

Reporting group title	MEDI3250
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	MEDI3250	Placebo	Total
Number of subjects	868	433	1301
Age Categorical			
Units: Subjects			
Children (2-11 years)	534	277	811
Adolescents (12-17 years)	314	145	459
Adults (18-64 years)	20	11	31
Age Continuous			
Units: years			
arithmetic mean	11	10.8	
standard deviation	± 3	± 2.8	-
Gender Categorical			
Units: Subjects			
Female	408	226	634
Male	460	207	667
Number of Doses of Study Vaccine Received			
Units: Subjects			
One	841	421	1262
Two	27	12	39
Prior Influenza Vaccination			
Units: Subjects			
Yes	788	386	1174
No	80	47	127

### Subject analysis sets

Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description: ITT	
Subject analysis set title	Safety analysis set
Subject analysis set type	Safety analysis
Subject analysis set description: Safety analysis set	
Subject analysis set title	PPS
Subject analysis set type	Per protocol
Subject analysis set description: PPS	

<b>Reporting group values</b>	ITT	Safety analysis set	PPS
Number of subjects	1301	1301	1279
Age Categorical Units: Subjects			
Children (2-11 years)	811	811	801
Adolescents (12-17 years)	459	459	449
Adults (18-64 years)	31	31	29
Age Continuous Units: years			
arithmetic mean	10.9	10.9	10.9
standard deviation	± 2.9	± 2.9	± 2.9
Gender Categorical Units: Subjects			
Female	634	634	622
Male	667	667	657
Number of Doses of Study Vaccine Received Units: Subjects			
One	1262	1262	1240
Two	39	39	39
Prior Influenza Vaccination Units: Subjects			
Yes	1174	1174	1153
No	127	127	126

## End points

### End points reporting groups

Reporting group title	MEDI3250
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	
Subject analysis set title	ITT
Subject analysis set type	Intention-to-treat
Subject analysis set description:	ITT
Subject analysis set title	Safety analysis set
Subject analysis set type	Safety analysis
Subject analysis set description:	Safety analysis set
Subject analysis set title	PPS
Subject analysis set type	Per protocol
Subject analysis set description:	PPS

### Primary: Influenza Attacked (Matched Strain)

End point title	Influenza Attacked (Matched Strain)
End point description:	
End point type	Primary
End point timeframe:	Until end of influenza surveillance period

End point values	MEDI3250	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	849	430		
Units: number	0	1		

### Statistical analyses

Statistical analysis title	Vaccine efficacy for matched strain
Comparison groups	MEDI3250 v Placebo
Number of subjects included in analysis	1279
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Vaccine Efficacy
Point estimate	100



Confidence interval	
level	95 %
sides	2-sided
lower limit	-1875.3
upper limit	100

### Secondary: Influenza Attacked (Any Strain)

End point title	Influenza Attacked (Any Strain)
End point description:	
End point type	Secondary
End point timeframe:	
Until end of influenza surveillance period	

End point values	MEDI3250	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	849	430		
Units: number	215	146		

### Statistical analyses

Statistical analysis title	Vaccine efficacy for any strain
Comparison groups	MEDI3250 v Placebo
Number of subjects included in analysis	1279
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Vaccine Efficacy
Point estimate	25.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	7.7
upper limit	39.8

### Secondary: Influenza Attacked (Matched Strain, by Strain)

End point title	Influenza Attacked (Matched Strain, by Strain)
End point description:	
End point type	Secondary
End point timeframe:	
Until end of influenza surveillance period	

<b>End point values</b>	MEDI3250	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	849	430		
Units: number				
Strain A/H1N1	0	0		
Strain A/H3N2	0	0		
Strain B/Yamagata	0	1		
Strain B/Victoria	0	0		

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

AEs were collected from Day 1 until the end of the influenza surveillance period.

Serious adverse events were collected from informed consent until the end of the influenza surveillance period.

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
Dictionary version	17.1

### Reporting groups

Reporting group title	MEDI3250
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Reporting group description:

Nasal spray administration of MEDI3250 0.2 mL (0.1 mL per nostril)

Reporting group title	Total
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Reporting group description:

Nasal spray administration of study drug 0.2 mL (0.1 mL per nostril)

Reporting group title	Placebo
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Reporting group description:

Nasal spray administration of Placebo 0.2 mL (0.1 mL per nostril)

Serious adverse events	MEDI3250	Total	Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 868 (0.35%)	6 / 1301 (0.46%)	3 / 433 (0.69%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Nervous system disorders			
Convulsion			
subjects affected / exposed	1 / 868 (0.12%)	1 / 1301 (0.08%)	0 / 433 (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
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	0 / 868 (0.00%)	1 / 1301 (0.08%)	1 / 433 (0.23%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Osteochondrosis			

subjects affected / exposed	0 / 868 (0.00%)	1 / 1301 (0.08%)	1 / 433 (0.23%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
<b>Infections and infestations</b>			
Appendicitis			
subjects affected / exposed	1 / 868 (0.12%)	1 / 1301 (0.08%)	0 / 433 (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
Peritonsillar abscess			
subjects affected / exposed	1 / 868 (0.12%)	1 / 1301 (0.08%)	0 / 433 (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
Pneumonia			
subjects affected / exposed	0 / 868 (0.00%)	1 / 1301 (0.08%)	1 / 433 (0.23%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

<b>Non-serious adverse events</b>	<b>MEDI3250</b>	<b>Total</b>	<b>Placebo</b>
Total subjects affected by non-serious adverse events			
subjects affected / exposed	133 / 868 (15.32%)	205 / 1301 (15.76%)	72 / 433 (16.63%)
<b>Gastrointestinal disorders</b>			
diarrhoea			
subjects affected / exposed	10 / 868 (1.15%)	15 / 1301 (1.15%)	5 / 433 (1.15%)
occurrences (all)	10	15	5
<b>Respiratory, thoracic and mediastinal disorders</b>			
Upper respiratory tract inflammation			
subjects affected / exposed	18 / 868 (2.07%)	26 / 1301 (2.00%)	8 / 433 (1.85%)
occurrences (all)	18	26	8
rhinorrhoea			
subjects affected / exposed	14 / 868 (1.61%)	23 / 1301 (1.77%)	9 / 433 (2.08%)
occurrences (all)	14	23	9
cough			

subjects affected / exposed occurrences (all)	7 / 868 (0.81%) 7	12 / 1301 (0.92%) 12	5 / 433 (1.15%) 5
phinitia allergic subjects affected / exposed occurrences (all)	9 / 868 (1.04%) 9	11 / 1301 (0.85%) 11	2 / 433 (0.46%) 2
Infections and infestations			
nasopharyngitis			
subjects affected / exposed occurrences (all)	70 / 868 (8.06%) 70	106 / 1301 (8.15%) 106	36 / 433 (8.31%) 36
bronchitis			
subjects affected / exposed occurrences (all)	5 / 868 (0.58%) 5	12 / 1301 (0.92%) 12	7 / 433 (1.62%) 7

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported