



## 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 |
|-----------------------|-------------|

##### 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,<br>Wilmington, DE, United States, 19850-5437                              |
| Public contact               | INformation Center, AstraZeneca Clinical Study Information<br>Center, 1+ 877-240-9479,<br>informationcenter@astrazeneca.com |
| Scientific contact           | Raburn Mallony, MedImmune, 1+ 301-398-0000,<br>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:

| <b>Subjects enrolled per age group</b>    |     |
|---|-----|
| 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 |
|----------------------------|---------------------------------|

### 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, Carer, Data analyst, 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 |
|------------------|---------|

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<br>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<br>Units: years                               |          |         |       |
| arithmetic mean  | 11       | 10.8    |       |
| standard deviation   | ± 3      | ± 2.8   | -     |
| Gender Categorical<br>Units: Subjects                        |          |         |       |
| Female   | 408      | 226     | 634   |
| Male   | 460      | 207     | 667   |
| Number of Doses of Study Vaccine Received<br>Units: Subjects |          |         |       |
| One  | 841      | 421     | 1262  |
| Two  | 27       | 12      | 39    |
| Prior Influenza Vaccination<br>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:<br>ITT                 |                     |
| Subject analysis set title                               | Safety analysis set |
| Subject analysis set type                                | Safety analysis     |
| Subject analysis set description:<br>Safety analysis set |                     |
| Subject analysis set title                               | PPS                 |
| Subject analysis set type                                | Per protocol        |
| Subject analysis set description:<br>PPS                 |                     |

| <b>Reporting group values</b>                                | ITT   | Safety analysis set | PPS   |
|--|-------|---------------------|-------|
| Number of subjects   | 1301  | 1301                | 1279  |
| Age Categorical<br>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<br>Units: years                               |       |                     |       |
| arithmetic mean  | 10.9  | 10.9                | 10.9  |
| standard deviation   | ± 2.9 | ± 2.9               | ± 2.9 |
| Gender Categorical<br>Units: Subjects                        |       |                     |       |
| Female   | 634   | 634                 | 622   |
| Male   | 667   | 667                 | 657   |
| Number of Doses of Study Vaccine Received<br>Units: Subjects |       |                     |       |
| One  | 1262  | 1262                | 1240  |
| Two  | 39    | 39                  | 39    |
| Prior Influenza Vaccination<br>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:<br>ITT                 |                     |
| Subject analysis set title                               | Safety analysis set |
| Subject analysis set type                                | Safety analysis     |
| Subject analysis set description:<br>Safety analysis set |                     |
| Subject analysis set title                               | PPS                 |
| Subject analysis set type                                | Per protocol        |
| Subject analysis set description:<br>PPS                 |                     |

### Primary: Influenza Attacked (Matched Strain)

|  |                                     |
|--|-------------------------------------|
| End point title  | Influenza Attacked (Matched Strain) |
| End point description:   |                                     |
|  |                                     |
| End point type   | Primary                             |
| End point timeframe:<br>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 |
|-----------------|----------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 17.1 |
|--------------------|------|

### Reporting groups

|                       |          |
|-----------------------|----------|
| Reporting group title | MEDI3250 |
|-----------------------|----------|

Reporting group description:

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

|                       |       |
|-----------------------|-------|
| Reporting group title | Total |
|-----------------------|-------|

Reporting group description:

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

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

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