



## Clinical trial results:

**A phase II, randomised, open-label study to evaluate the safety and immunogenicity of the adjuvanted pandemic H1N1 influenza candidate vaccine following a 0-28 day or 0-4 month vaccination schedule in subjects aged 8 to 12 weeks.**

### Summary

|                          |                  |
|--------------------------|------------------|
| EudraCT number           | 2009-015174-35   |
| Trial protocol           | NO               |
| Global end of trial date | 25 November 2010 |

### Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v1            |
| This version publication date  | 18 April 2016 |
| First version publication date | 13 June 2015  |

### Trial information

#### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 113629 |
|-----------------------|--------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01003418 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |                                                                                                         |
|------------------------------|---------------------------------------------------------------------------------------------------------|
| Sponsor organisation name    | GlaxoSmithKline Biologicals                                                                             |
| Sponsor organisation address | Rue de l'Institut 89, Rixensart, Belgium,                                                               |
| Public contact               | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com |
| Scientific contact           | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com |

Notes:

### Paediatric regulatory details

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

Notes:

## Results analysis stage

|                                                      |                  |
|------------------------------------------------------|------------------|
| Analysis stage                                       | Final            |
| Date of interim/final analysis                       | 25 November 2010 |
| Is this the analysis of the primary completion data? | No               |
| Global end of trial reached?                         | Yes              |
| Global end of trial date                             | 25 November 2010 |
| Was the trial ended prematurely?                     | Yes              |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the safety and reactogenicity of the H1N1 candidate vaccine in terms of solicited local and general symptoms, unsolicited adverse events (AEs) and serious adverse events (SAEs) two weeks post Dose 1.

Protection of trial subjects:

The vaccinees were observed closely for at least 30 minutes, with appropriate medical treatment readily available in case of anaphylaxis following the administration of vaccines.

Background therapy: -

Evidence for comparator: -

|                                                           |                  |
|-----------------------------------------------------------|------------------|
| Actual start date of recruitment                          | 17 November 2009 |
| 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 | Norway: 8 |
| Worldwide total number of subjects   | 8         |
| EEA total number of subjects         | 8         |

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)  | 8 |
| Children (2-11 years)                     | 0 |
| 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:

Only 8 subjects were enrolled in the study as the study was prematurely terminated for logistic reasons.

### Pre-assignment

Screening details:

During the screening the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical history of the subjects and signing informed consent forms.

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall Study (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Randomised - controlled        |
| Blinding used                | Not blinded                    |

### Arms

|                              |             |
|------------------------------|-------------|
| Are arms mutually exclusive? | Yes         |
| <b>Arm title</b>             | Flu A Group |

Arm description:

Subjects received 2 primary doses of H1N1 vaccine, according to a 0-28 day schedule. Subjects also received routine infant immunisation (DTPa-IPV/Hib) and 7Pn vaccine at Day 14, Month 3 and Month 10.

|                                        |                                                                                                                           |
|----------------------------------------|---------------------------------------------------------------------------------------------------------------------------|
| Arm type                               | Experimental                                                                                                              |
| Investigational medicinal product name | Pandemrix™                                                                                                                |
| Investigational medicinal product code | GSK2340272A                                                                                                               |
| Other name                             | A/California/7/2009 (H1N1)v-like vaccine adjuvanted with AS03, Split virion, inactivated A/California/7/2009 (H1N1)v-like |
| Pharmaceutical forms                   | Emulsion for injection                                                                                                    |
| Routes of administration               | Intramuscular use                                                                                                         |

Dosage and administration details:

2 primary doses of H1N1 vaccine administered intramuscularly in the anterolateral region of the left thigh at Day 0 and right thigh at Day 28.

|                                        |                        |
|----------------------------------------|------------------------|
| Investigational medicinal product name | Infanrix™ -IPV+HIB     |
| Investigational medicinal product code |                        |
| Other name                             | DTPa-IPV/Hib           |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Intramuscular use      |

Dosage and administration details:

3 doses administered intramuscularly at Day 14, Month 3 and Month 10 in anterolateral region of right thigh.

|                                        |                                         |
|----------------------------------------|-----------------------------------------|
| Investigational medicinal product name | Prevenar™                               |
| Investigational medicinal product code |                                         |
| Other name                             | 7-valent pneumococcal conjugate vaccine |
| Pharmaceutical forms                   | Solution for injection                  |
| Routes of administration               | Intramuscular use                       |

Dosage and administration details:

3 doses administered intramuscularly in the anterolateral region of left thigh at at Day 14, Month 3 and Month 10.

|                  |             |
|------------------|-------------|
| <b>Arm title</b> | Flu B Group |
|------------------|-------------|

Arm description:

Subjects received 2 primary doses of H1N1 vaccine, according to a 0-4 month schedule. Subjects also received routine infant immunisation (DTPa-IPV/Hib) and 7Pn vaccine at Day 14, Month 3 and Month 10.

|          |              |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

|                                        |                                                                                                                           |
|----------------------------------------|---------------------------------------------------------------------------------------------------------------------------|
| Investigational medicinal product name | Pandemrix™                                                                                                                |
| Investigational medicinal product code | GSK2340272A                                                                                                               |
| Other name                             | A/California/7/2009 (H1N1)v-like vaccine adjuvanted with AS03, Split virion, inactivated A/California/7/2009 (H1N1)v-like |
| Pharmaceutical forms                   | Emulsion for injection                                                                                                    |
| Routes of administration               | Intramuscular use                                                                                                         |

Dosage and administration details:

2 primary doses of H1N1 vaccine administered intramuscularly in the anterolateral region of the left thigh at Day 0 and right thigh at Month 4.

|                                        |                        |
|----------------------------------------|------------------------|
| Investigational medicinal product name | Infanrix™ -IPV+HIB     |
| Investigational medicinal product code |                        |
| Other name                             | DTPa-IPV/Hib           |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Intramuscular use      |

Dosage and administration details:

3 doses administered intramuscularly at Day 14, Month 3 and Month 10 in anterolateral region of right thigh.

|                                        |                                         |
|----------------------------------------|-----------------------------------------|
| Investigational medicinal product name | Prevenar™                               |
| Investigational medicinal product code |                                         |
| Other name                             | 7-valent pneumococcal conjugate vaccine |
| Pharmaceutical forms                   | Solution for injection                  |
| Routes of administration               | Intramuscular use                       |

Dosage and administration details:

3 doses administered intramuscularly in the anterolateral region of left thigh at at Day 14, Month 3 and Month 10.

| <b>Number of subjects in period 1</b> | Flu A Group | Flu B Group |
|---------------------------------------|-------------|-------------|
| Started                               | 5           | 3           |
| Completed                             | 5           | 3           |

## Baseline characteristics

### Reporting groups

|                       |             |
|-----------------------|-------------|
| Reporting group title | Flu A Group |
|-----------------------|-------------|

Reporting group description:

Subjects received 2 primary doses of H1N1 vaccine, according to a 0-28 day schedule. Subjects also received routine infant immunisation (DTPa-IPV/Hib) and 7Pn vaccine at Day 14, Month 3 and Month 10.

|                       |             |
|-----------------------|-------------|
| Reporting group title | Flu B Group |
|-----------------------|-------------|

Reporting group description:

Subjects received 2 primary doses of H1N1 vaccine, according to a 0-4 month schedule. Subjects also received routine infant immunisation (DTPa-IPV/Hib) and 7Pn vaccine at Day 14, Month 3 and Month 10.

| Reporting group values                             | Flu A Group | Flu B Group | Total |
|----------------------------------------------------|-------------|-------------|-------|
| Number of subjects                                 | 5           | 3           | 8     |
| 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                                     |             |             |       |
| Standard deviation data was not available.         |             |             |       |
| Units: weeks                                       |             |             |       |
| arithmetic mean                                    | 9           | 8           |       |
| standard deviation                                 | ± 0         | ± 0         | -     |
| Gender categorical                                 |             |             |       |
| Units: Subjects                                    |             |             |       |
| Female                                             | 4           | 2           | 6     |
| Male                                               | 1           | 1           | 2     |

## End points

### End points reporting groups

|                                                                                                                                                                                                          |             |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------|
| Reporting group title                                                                                                                                                                                    | Flu A Group |
| Reporting group description:                                                                                                                                                                             |             |
| Subjects received 2 primary doses of H1N1 vaccine, according to a 0-28 day schedule. Subjects also received routine infant immunisation (DTPa-IPV/Hib) and 7Pn vaccine at Day 14, Month 3 and Month 10.  |             |
| Reporting group title                                                                                                                                                                                    | Flu B Group |
| Reporting group description:                                                                                                                                                                             |             |
| Subjects received 2 primary doses of H1N1 vaccine, according to a 0-4 month schedule. Subjects also received routine infant immunisation (DTPa-IPV/Hib) and 7Pn vaccine at Day 14, Month 3 and Month 10. |             |

### Primary: Number of subjects with any, grade 3 and related unsolicited adverse events (AEs).

|                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |                                                                                                   |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | Number of subjects with any, grade 3 and related unsolicited adverse events (AEs). <sup>[1]</sup> |
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                   |
| An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination. Grade 3 AE = an AE which prevented normal, everyday activities/crying that cannot be comforted. Related = AE assessed by the investigator as related to the vaccination.<br>The data was not analyzed as the study was prematurely terminated and due to recruitment issues. |                                                                                                   |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 | Primary                                                                                           |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |                                                                                                   |
| 2 weeks post-Dose 1 (Day 0 and Day 13)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |                                                                                                   |

Notes:

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

Justification: The study was terminated prematurely for logistic reasons not related to safety or efficacy of the vaccine; only eight subjects were enrolled in the study. Therefore, no statistical analyses were conducted.

| End point values            | Flu A Group      | Flu B Group      |  |  |
|-----------------------------|------------------|------------------|--|--|
| Subject group type          | Reporting group  | Reporting group  |  |  |
| Number of subjects analysed | 0 <sup>[2]</sup> | 0 <sup>[3]</sup> |  |  |
| Units: Number               |                  |                  |  |  |

Notes:

[2] - The data was not analyzed as the study was prematurely terminated and due to recruitment issues.

[3] - The data was not analyzed as the study was prematurely terminated and due to recruitment issues.

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects with any, grade 3 and related unsolicited AEs

|                                                                                                         |                                                                  |
|---------------------------------------------------------------------------------------------------------|------------------------------------------------------------------|
| End point title                                                                                         | Number of subjects with any, grade 3 and related unsolicited AEs |
| End point description:                                                                                  |                                                                  |
| An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally |                                                                  |

associated with the use of a medicinal product, whether or not considered related to the medicinal product and reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any AE reported in addition to those solicited during the clinical study. Also any 'solicited' symptom with onset outside the specified period of follow-up for solicited symptoms will be reported as an unsolicited AE. Any was defined as the occurrence of any unsolicited AE regardless of intensity grade or relation to vaccination. Grade 3 AE = an AE which prevented normal, everyday activities/crying that cannot be comforted. Related = AE assessed by the investigator as related to the vaccination.

|                                                                                        |           |
|----------------------------------------------------------------------------------------|-----------|
| End point type                                                                         | Secondary |
| End point timeframe:                                                                   |           |
| During the 28-day (Days 0-27) follow-up period after each H1N1 vaccine administration. |           |

| End point values            | Flu A Group     | Flu B Group     |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 5               | 3               |  |  |
| Units: Subjects             |                 |                 |  |  |
| Any AE(s)                   | 3               | 2               |  |  |
| Grade 3 AE(s)               | 0               | 0               |  |  |
| Related AE(s)               | 0               | 0               |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects with serious adverse events (SAEs).

|                                                                                                                                                                                             |                                                        |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------|
| End point title                                                                                                                                                                             | Number of subjects with serious adverse events (SAEs). |
| End point description:                                                                                                                                                                      |                                                        |
| SAEs assessed included medical occurrences that resulted in death, were life threatening, required hospitalization or prolongation of hospitalization or resulted in disability/incapacity. |                                                        |
| End point type                                                                                                                                                                              | Secondary                                              |
| End point timeframe:                                                                                                                                                                        |                                                        |
| During the entire study period (Day 0 - Month 11)                                                                                                                                           |                                                        |

| End point values            | Flu A Group     | Flu B Group     |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 5               | 3               |  |  |
| Units: Subjects             |                 |                 |  |  |
| Any SAE(s)                  | 0               | 0               |  |  |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Unsolicited AEs: Within 28-day follow-up period after each H1N1 vaccination. SAEs: Throughout the entire study (Day 0 to Month 11).

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 13.1 |
|--------------------|------|

### Reporting groups

|                       |             |
|-----------------------|-------------|
| Reporting group title | Flu A Group |
|-----------------------|-------------|

Reporting group description:

Subjects received 2 primary doses of H1N1 vaccine, according to a 0-28 day schedule. Subjects also received routine infant immunisation (DTPa-IPV/Hib) and 7Pn vaccine at Day 14, Month 3 and Month 10.

|                       |             |
|-----------------------|-------------|
| Reporting group title | Flu B Group |
|-----------------------|-------------|

Reporting group description:

Subjects received 2 primary doses of H1N1 vaccine, according to a 0-4 month schedule. Subjects also received routine infant immunisation (DTPa-IPV/Hib) and 7Pn vaccine at Day 14, Month 3 and Month 10.

| Serious adverse events                            | Flu A Group   | Flu B Group   |  |
|---------------------------------------------------|---------------|---------------|--|
| Total subjects affected by serious adverse events |               |               |  |
| subjects affected / exposed                       | 0 / 5 (0.00%) | 0 / 3 (0.00%) |  |
| number of deaths (all causes)                     | 0             | 0             |  |
| number of deaths resulting from adverse events    |               |               |  |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events                            | Flu A Group    | Flu B Group    |  |
|-------------------------------------------------------|----------------|----------------|--|
| Total subjects affected by non-serious adverse events |                |                |  |
| subjects affected / exposed                           | 3 / 5 (60.00%) | 2 / 3 (66.67%) |  |
| Respiratory, thoracic and mediastinal disorders       |                |                |  |
| Cough                                                 |                |                |  |
| subjects affected / exposed                           | 1 / 5 (20.00%) | 1 / 3 (33.33%) |  |
| occurrences (all)                                     | 1              | 1              |  |
| Tracheal inflammation                                 |                |                |  |
| subjects affected / exposed                           | 1 / 5 (20.00%) | 0 / 3 (0.00%)  |  |
| occurrences (all)                                     | 1              | 0              |  |
| Infections and infestations                           |                |                |  |

|                             |                |                |  |
|-----------------------------|----------------|----------------|--|
| Nasopharyngitis             |                |                |  |
| subjects affected / exposed | 1 / 5 (20.00%) | 1 / 3 (33.33%) |  |
| occurrences (all)           | 1              | 2              |  |
| Conjunctivitis              |                |                |  |
| subjects affected / exposed | 1 / 5 (20.00%) | 0 / 3 (0.00%)  |  |
| occurrences (all)           | 1              | 0              |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment                                                                                                                                                                                                                                                                                                |
|------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 01 December 2009 | On request of Paediatric Committee (PDCO)/Committee for Medicinal Products for Human Use (CHMP), reporting of vaccine effectiveness and vaccine failure were incorporated. One telephone contact per group was added after the second dose to monitor fever, based on previous paediatric study results. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date             | Interruption                                                                                                                                                | Restart date |
|------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------|
| 25 November 2010 | The study was terminated prematurely for logistic reasons not related to safety or efficacy of the vaccine; only eight subjects were enrolled in the study. | -            |

Notes:

### Limitations and caveats

None reported