



## Clinical trial results:

**A Phase I, double-blind, randomised, placebo controlled study to evaluate the reactogenicity and safety of a single oral dose of GlaxoSmithKline (GSK) Biologicals' live attenuated liquid human rotavirus (HRV) vaccine in healthy children aged 2 to 6 years in China.**

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2015-001547-37 |
| Trial protocol           | Outside EU/EEA |
| Global end of trial date | 16 April 2010  |

### Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v1 (current)  |
| This version publication date  | 20 April 2016 |
| First version publication date | 17 July 2015  |

### Trial information

#### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 113552 |
|-----------------------|--------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01086436 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | GlaxoSmithKline Biologicals   |
| Sponsor organisation address | Rue de l'Institut 89, Rixensart, Belgium, B-1330  |
| Public contact               | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalsupportHD@gsk.com |
| Scientific contact           | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, 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:

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**Results analysis stage**

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|  |               |
|--|---------------|
| Analysis stage                                       | Final         |
| Date of interim/final analysis                       | 28 July 2010  |
| Is this the analysis of the primary completion data? | Yes           |
| Primary completion date                              | 16 April 2010 |
| Global end of trial reached?                         | Yes           |
| Global end of trial date                             | 16 April 2010 |
| Was the trial ended prematurely?                     | No            |

Notes:

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**General information about the trial**

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Main objective of the trial:

To assess the reactogenicity of a single oral dose of GSK Biologicals' liquid HRV vaccine when compared to placebo group, in terms of solicited AEs in healthy children aged 2 to 6 years

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

|   |               |
|---|---------------|
| Actual start date of recruitment                          | 13 March 2010 |
| Long term follow-up planned                               | No            |
| Independent data monitoring committee (IDMC) involvement? | No            |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |           |
|--------------------------------------|-----------|
| Country: Number of subjects enrolled | China: 50 |
| Worldwide total number of subjects   | 50        |
| EEA total number of subjects         | 0         |

Notes:

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**Subjects enrolled per age group**

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|   |    |
|---|----|
| 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)                     | 50 |
| 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: -

### 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                | Double blind                           |
| Roles blinded                | Subject, Investigator, Carer, Assessor |

### Arms

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

Arm description:

Subjects received a single oral dose of GSK Biologicals' oral live attenuated liquid human rotavirus vaccine (HRV) vaccine at Day 0

|  |  |
|--|--|
| Arm type                               | Experimental                                     |
| Investigational medicinal product name | Rotarix  |
| Investigational medicinal product code |  |
| Other name                             | HUMAN ROTAVIRUS RIX4414 STRAIN (LIVE ATTENUATED) |
| Pharmaceutical forms                   | Powder and solvent for oral suspension           |
| Routes of administration               | Oral use   |

Dosage and administration details:

One dose of HRV vaccine administered orally at Day 0.

|                  |               |
|------------------|---------------|
| <b>Arm title</b> | Placebo Group |
|------------------|---------------|

Arm description:

Subjects received a single oral dose of placebo at Day 0

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Placebo      |
| Investigational medicinal product code |              |
| Other name                             |              |
| Pharmaceutical forms                   | Injection    |
| Routes of administration               | Oral use     |

Dosage and administration details:

One dose of placebo administered orally at Day 0

| <b>Number of subjects in period 1</b> | HRV Group | Placebo Group |
|---------------------------------------|-----------|---------------|
| Started                               | 25        | 25            |
| Completed                             | 25        | 25            |

## Baseline characteristics

### Reporting groups

|   |               |
|---|---------------|
| Reporting group title   | HRV Group     |
| Reporting group description:<br>Subjects received a single oral dose of GSK Biologicals' oral live attenuated liquid human rotavirus vaccine (HRV) vaccine at Day 0 |               |
| Reporting group title   | Placebo Group |
| Reporting group description:<br>Subjects received a single oral dose of placebo at Day 0  |               |

| Reporting group values                                | HRV Group | Placebo Group | Total |
|---|-----------|---------------|-------|
| Number of subjects                                    | 25        | 25            | 50    |
| Age categorical<br>Units: Subjects                    |           |               |       |
| In utero  |           |               | 0     |
| Preterm newborn infants<br>(gestational age < 37 wks) |           |               | 0     |
| Newborns (0-27 days)                                  |           |               | 0     |
| Infants and toddlers (28 days-23<br>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<br>Units: years                        |           |               |       |
| arithmetic mean                                       | 3.7       | 3.9           |       |
| standard deviation                                    | ± 0.89    | ± 0.97        | -     |
| Gender categorical<br>Units: Subjects                 |           |               |       |
| Female  | 9         | 16            | 25    |
| Male  | 16        | 9             | 25    |

## End points

### End points reporting groups

|   |               |
|---|---------------|
| Reporting group title   | HRV Group     |
| Reporting group description:  |               |
| Subjects received a single oral dose of GSK Biologicals' oral live attenuated liquid human rotavirus vaccine (HRV) vaccine at Day 0 |               |
| Reporting group title   | Placebo Group |
| Reporting group description:  |               |
| Subjects received a single oral dose of placebo at Day 0  |               |

### Primary: Number of subjects reporting any, grade 3 and related solicited general symptoms

|                 |   |
|-----------------|---|
| End point title | Number of subjects reporting any, grade 3 and related solicited general symptoms <sup>[1]</sup> |
|-----------------|---|

#### End point description:

Assessed solicited general symptoms were cough, diarrhea, irritability, loss of appetite, fever (According to Chinese scale and GSK scale) and vomiting.

Any = occurrence of the symptom regardless of intensity grade or relationship to study vaccination.

Grade 3 Cough = Cough/runny nose which prevented daily activity. Grade 3 Diarrhea =  $\geq 6$  looser than normal stools/day. Grade 3 Irritability = Crying that could not be comforted/ prevented normal activity. Grade 3 Loss of appetite = Did not eat at all. Grade 3 fever (axillary temperature) =  $>39.0^{\circ}\text{C}$  according to both the Chinese and GSK scales. Grade 3 Vomiting =  $\geq 3$  episodes of vomiting/day. Related = symptom assessed by the investigator as related to the vaccination.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

#### End point timeframe:

During the 8-day (Days 0-7) post-vaccination period

#### 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 analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed

| End point values                    | HRV Group       | Placebo Group   |  |  |
|-------------------------------------|-----------------|-----------------|--|--|
| Subject group type                  | Reporting group | Reporting group |  |  |
| Number of subjects analysed         | 25              | 25              |  |  |
| Units: Subjects                     |                 |                 |  |  |
| Any Cough                           | 10              | 12              |  |  |
| Grade 3 Cough                       | 0               | 0               |  |  |
| Related Cough                       | 0               | 1               |  |  |
| Any Diarrhea                        | 1               | 1               |  |  |
| Grade 3 Diarrhea                    | 0               | 1               |  |  |
| Related Diarrhea                    | 1               | 0               |  |  |
| Any Irritability                    | 3               | 2               |  |  |
| Grade 3 Irritability                | 0               | 0               |  |  |
| Related Irritability                | 0               | 0               |  |  |
| Any Loss of appetite                | 2               | 3               |  |  |
| Grade 3 Loss of appetite            | 0               | 0               |  |  |
| Related Loss of appetite            | 0               | 0               |  |  |
| Any temperature (Chinese scale)     | 4               | 5               |  |  |
| Grade 3 temperature (Chinese scale) | 0               | 0               |  |  |

|                                     |   |   |  |  |
|-------------------------------------|---|---|--|--|
| Related temperature (Chinese scale) | 0 | 1 |  |  |
| Any temperature (GSK scale)         | 1 | 2 |  |  |
| Grade 3 temperature (GSK scale)     | 0 | 0 |  |  |
| Related temperature (GSK scale)     | 0 | 1 |  |  |
| Any Vomiting                        | 1 | 0 |  |  |
| Grade 3 Vomiting                    | 0 | 0 |  |  |
| Related Vomiting                    | 0 | 0 |  |  |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects reporting any unsolicited adverse event (AE)

|                 |   |
|-----------------|---|
| End point title | Number of subjects reporting any unsolicited adverse event (AE) |
|-----------------|---|

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. Any was defined as an adverse event (AE) reported in addition to those solicited during the clinical study period of one month (Day 0 – Day 30). Also, any solicited symptom with onset outside the specified period of follow-up for solicited symptoms will be reported as an unsolicited adverse event.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Within 31 days (Day 0 - Day 30) after the HRV vaccine/placebo dose

| End point values            | HRV Group       | Placebo Group   |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 25              | 25              |  |  |
| Units: Subjects             |                 |                 |  |  |
| Any AE(s)                   | 11              | 13              |  |  |

## 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:

Serious adverse events (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 to Month 1)

|                             |                 |                 |  |  |
|-----------------------------|-----------------|-----------------|--|--|
| <b>End point values</b>     | HRV Group       | Placebo Group   |  |  |
| Subject group type          | Reporting group | Reporting group |  |  |
| Number of subjects analysed | 25              | 25              |  |  |
| 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:

Solicited symptoms were collected during the 8-day (Days 0-7) post vaccination period. Unsolicited AEs were collected during the 31-day (Days 0-30) post vaccination period. SAEs were collected during the entire study period (Day 0 - Month 1).

Adverse event reporting additional description:

The number of occurrences reported for solicited symptoms, adverse events, and serious adverse events were not available for posting. The number of subjects affected by each specific event was indicated as the number of occurrences.

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 13.0 |
|--------------------|------|

### Reporting groups

|                       |           |
|-----------------------|-----------|
| Reporting group title | HRV Group |
|-----------------------|-----------|

Reporting group description:

Subjects received a single oral dose of GSK Biologicals' oral live attenuated liquid human rotavirus vaccine (HRV) vaccine at Day 0

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

Reporting group description:

Subjects received a single oral dose of placebo at Day 0

| Serious adverse events                            | HRV Group      | Placebo Group  |  |
|---|----------------|----------------|--|
| Total subjects affected by serious adverse events |                |                |  |
| subjects affected / exposed                       | 0 / 25 (0.00%) | 0 / 25 (0.00%) |  |
| number of deaths (all causes)                     | 0              | 0              |  |
| number of deaths resulting from adverse events    | 0              | 0              |  |

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

| Non-serious adverse events                            | HRV Group         | Placebo Group     |  |
|---|-------------------|-------------------|--|
| Total subjects affected by non-serious adverse events |                   |                   |  |
| subjects affected / exposed                           | 25 / 25 (100.00%) | 25 / 25 (100.00%) |  |
| General disorders and administration site conditions  |                   |                   |  |
| Cough (solicited)                                     |                   |                   |  |
| alternative assessment type: Systematic               |                   |                   |  |
| subjects affected / exposed                           | 10 / 25 (40.00%)  | 12 / 25 (48.00%)  |  |
| occurrences (all)                                     | 10                | 12                |  |
| Diarrhea  |                   |                   |  |

|  |                      |                      |  |
|--|----------------------|----------------------|--|
| alternative assessment type:<br>Systematic<br>subjects affected / exposed<br>occurrences (all)                             | 1 / 25 (4.00%)<br>1  | 1 / 25 (4.00%)<br>1  |  |
| Irritability<br>alternative assessment type:<br>Systematic<br>subjects affected / exposed<br>occurrences (all)             | 3 / 25 (12.00%)<br>3 | 2 / 25 (8.00%)<br>2  |  |
| Loss of appetite<br>alternative assessment type:<br>Systematic<br>subjects affected / exposed<br>occurrences (all)         | 2 / 25 (8.00%)<br>2  | 3 / 25 (12.00%)<br>3 |  |
| Fever (Chinese scale)<br>alternative assessment type:<br>Systematic<br>subjects affected / exposed<br>occurrences (all)    | 4 / 25 (16.00%)<br>4 | 5 / 25 (20.00%)<br>5 |  |
| Fever (GSK scale)<br>alternative assessment type:<br>Systematic<br>subjects affected / exposed<br>occurrences (all)        | 1 / 25 (4.00%)<br>1  | 2 / 25 (8.00%)<br>2  |  |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)  | 3 / 25 (12.00%)<br>3 | 1 / 25 (4.00%)<br>1  |  |
| Respiratory, thoracic and mediastinal disorders<br>Cough (unsolicited)<br>subjects affected / exposed<br>occurrences (all) | 3 / 25 (12.00%)<br>3 | 5 / 25 (20.00%)<br>5 |  |
| Rhinorrhoea<br>subjects affected / exposed<br>occurrences (all)  | 0 / 25 (0.00%)<br>0  | 2 / 25 (8.00%)<br>2  |  |
| Infections and infestations<br>Nasopharyngitis<br>subjects affected / exposed<br>occurrences (all)                         | 3 / 25 (12.00%)<br>3 | 4 / 25 (16.00%)<br>4 |  |

## **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