# Clinical trial results:
# A phase IIIb, double blind, randomised, placebo–controlled, multi–country, multicentre study to assess the safety, reactogenicity and immunogenicity of two doses of GlaxoSmithKline (GSK) Biologicals' oral live attenuated Human Rotavirus (HRV) Vaccine in pre–term infants.

## Summary

| | |
|---|---|
| EudraCT number | 2006-003762-33 |
| Trial protocol | FR PT ES |
| Global end of trial date | 31 March 2008 |

**Results information**

| | |
|---|---|
| Result version number | v1 |
| This version publication date | 11 May 2016 |
| First version publication date | 18 December 2014 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | 106481 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00420745 |
| 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, 044 2089904466, GSKClinicalSupportHD@gsk.com |
| Scientific contact | Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 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? | Yes |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 31 March 2008 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 31 March 2008 |
| Global end of trial reached? | Yes |
| Global end of trial date | 31 March 2008 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To assess the safety of GSK Biologicals' HRV vaccine in terms of occurrence of serious adverse events (SAEs), throughout the study period in pre–term infants receiving HRV vaccine versus pre–term infants receiving placebo.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 25 January 2007 |
| 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 | Poland: 435 |
| Country: Number of subjects enrolled | Portugal: 142 |
| Country: Number of subjects enrolled | Spain: 354 |
| Country: Number of subjects enrolled | France: 78 |
| Worldwide total number of subjects | 1009 |
| EEA total number of subjects | 1009 |

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) | 1009 |
| 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, Monitor |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Rotarix Group |

Arm description:

All subjects received 2 oral doses of Rotarix vaccine, 1 dose at Day 0 and 1 dose at Month 1 or 2 depending on the country.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Rotarix™ |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Oral suspension |
| Routes of administration | Oral use |

Dosage and administration details:

Two-dose oral vaccination.

| | |
|---|---|
| **Arm title** | Placebo Group |

Arm description:

All subjects received 2 oral doses of placebo, 1 dose at Day 0 and 1 dose at Month 1 or 2 depending on the country.

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

Dosage and administration details:

Two-dose oral administration.

| **Number of subjects in period 1** | Rotarix Group | Placebo Group |
|---|---|---|
| Started | 670 | 339 |
| Completed | 655 | 333 |
| Not completed | 15 | 6 |
| Physician decision | 1 | 1 |
| Adverse event, non-fatal | 2 | 2 |
| Recurrent pneumonia & bronchitis | - | 1 |
| Lost to follow-up | 10 | 2 |
| Protocol deviation | 1 | - |
| Age limit exceeded for Dose 2 | 1 | - |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Rotarix Group |
| Reporting group description: | |
| All subjects received 2 oral doses of Rotarix vaccine, 1 dose at Day 0 and 1 dose at Month 1 or 2 depending on the country. | |
| Reporting group title | Placebo Group |
| Reporting group description: | |
| All subjects received 2 oral doses of placebo, 1 dose at Day 0 and 1 dose at Month 1 or 2 depending on the country. | |

| Reporting group values | Rotarix Group | Placebo Group | Total |
|---|---|---|---|
| Number of subjects | 670 | 339 | 1009 |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | | 0 |
| Preterm newborn infants (gestational age < 37 wks) | | | 0 |
| Newborns (0-27 days) | | | 0 |
| Infants and toddlers (28 days-23 months) | | | 0 |
| Children (2-11 years) | | | 0 |
| Adolescents (12-17 years) | | | 0 |
| Adults (18-64 years) | | | 0 |
| From 65-84 years | | | 0 |
| 85 years and over | | | 0 |
| Age continuous | | | |
| Units: weeks | | | |
| geometric mean | 8.5 | 8.5 | |
| standard deviation | ± 1.77 | ± 1.78 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 327 | 167 | 494 |
| Male | 343 | 172 | 515 |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Rotarix Group |

Reporting group description:

All subjects received 2 oral doses of Rotarix vaccine, 1 dose at Day 0 and 1 dose at Month 1 or 2 depending on the country.

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

Reporting group description:

All subjects received 2 oral doses of placebo, 1 dose at Day 0 and 1 dose at Month 1 or 2 depending on the country.

### Primary: Number of Subjects Reporting Any Serious Adverse Events (SAEs).

| | |
|---|---|
| End point title | Number of Subjects Reporting Any Serious Adverse Events (SAEs).[1] |

End point description:

An SAE is any untoward medical occurrence that: results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect in the offspring of a study subject, or may evolve into one of the outcomes listed above.

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

End point timeframe:

From Day 0 up to 1 month after Dose 2 of Rotarix vaccine/Placebo

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 | Rotarix Group | Placebo Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 670 | 339 | | |
| Units: Subjects | | | | |
| (SAEs) | 34 | 23 | | |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of Subjects Reporting Unsolicited Adverse Events (AEs), According to Medical Dictionary for Regulatory Activities (MedDRA) Classification

| | |
|---|---|
| End point title | Number of Subjects Reporting Unsolicited Adverse Events (AEs), According to Medical Dictionary for Regulatory Activities (MedDRA) Classification |

End point description:

An AE is 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.

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

End point timeframe:

Within 31 days after any Rotarix vaccine/Placebo dose.

| End point values | Rotarix Group | Placebo Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 670 | 339 | | |
| Units: Subjects | 196 | 138 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects for whom each type of solicited symptom was reported.

| End point title | Number of subjects for whom each type of solicited symptom was reported. |
|---|---|

End point description:

Solicited symptoms included Diarrhea (3 or more looser than normal stools/day), Fever (axillary temperature ≥ 37.5 degrees Celsius (°C)), Irritability, Loss of appetite, and Vomiting

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

End point timeframe:

Within 15 days after each Rotarix vaccine/Placebo dose.

| End point values | Rotarix Group | Placebo Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 203 | 100 | | |
| Units: Subjects | | | | |
| Diarrhea | 9 | 5 | | |
| Fever | 54 | 29 | | |
| Irritability | 133 | 66 | | |
| Loss of appetite | 81 | 45 | | |
| Vomiting | 52 | 27 | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects for whom presence of rotavirus (RV) gastroenteritis (GE) was detected in stools.

| End point title | Number of subjects for whom presence of rotavirus (RV) gastroenteritis (GE) was detected in stools. |
|---|---|

End point description:

Gastroenteritis (GE): diarrhoea with or without vomiting. Rotavirus (RV) GE: A GE episode was a RV GE if a stool sample taken during or not later than 7 days after the episode was RV positive by Enzyme Linked Immunosorbent Assay.

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

End point timeframe:

From Dose 1 up to 1 month after Dose 2 of Rotarix vaccine/Placebo

| **End point values** | Rotarix Group | Placebo Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 670 | 339 | | |
| Units: Subjects | | | | |
| Number of subjects with RV | 3 | 2 | | |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Seroconversion to anti-rotavirus Immunoglobulin A (IgA) antibody.**

| End point title | Seroconversion to anti-rotavirus Immunoglobulin A (IgA) antibody. |
|---|---|

End point description:

Number of subjects with anti-rotavirus IgA antibody concentration ≥ 20 Units/milliliter (U/mL).

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

End point timeframe:

At Visit 3, 1 month after Dose 2 of Rotarix vaccine/Placebo

| **End point values** | Rotarix Group | Placebo Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 147 | 81 | | |
| Units: Subjects | | | | |
| Seroconversion to anti-rotavirus IgA | 126 | 13 | | |

**Statistical analyses**

No statistical analyses for this end point

**Secondary: Serum anti–rotavirus IgA antibody concentration.**

| End point title | Serum anti–rotavirus IgA antibody concentration. |
|---|---|

End point description:

Anti-rotavirus IgA antibody concentrations are given as geometric mean concentrations (GMC) with 95%

Confidence Intervals, calculated on all subjects.

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

End point timeframe:

At Visit 3, 1 month after Dose 2 of Rotarix vaccine/Placebo

| **End point values** | Rotarix Group | Placebo Group | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 147 | 81 | | |
| Units: U/mL | | | | |
| geometric mean (confidence interval 95%) | | | | |
| Serum anti–rotavirus IgA | 202.2 (153.1 to 267.1) | 0 (0 to 0) | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Serious Adverse events (SAE) = During the entire study period. Solicited local and general symptoms = Within 15 days (Day 0–Day 14) after each HRV vaccine/placebo dose. Unsolicited AEs = Within 31 days (Day 0–Day 30) after any HRV vaccine/placebo dose.

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 | 11 |

### Reporting groups

| | |
|---|---|
| Reporting group title | Rotarix Group |

Reporting group description:

All subjects received 2 oral doses of Rotarix vaccine, 1 dose at Day 0 and 1 dose at Month 1 or 2 depending on the country.

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

Reporting group description:

All subjects received 2 oral doses of placebo, 1 dose at Day 0 and 1 dose at Month 1 or 2 depending on the country.

| Serious adverse events | Rotarix Group | Placebo Group | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 34 / 670 (5.07%) | 23 / 339 (6.78%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |
| Congenital, familial and genetic disorders | | | |
| Coarctation of the aorta | | | |
| subjects affected / exposed | 1 / 670 (0.15%) | 0 / 339 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 670 (0.00%) | 2 / 339 (0.59%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |

| | | | |
|---|---|---|---|
| Pyrexia | | | |
| subjects affected / exposed | 4 / 670 (0.60%) | 3 / 339 (0.88%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 2 / 670 (0.30%) | 0 / 339 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea haemorrhagic | | | |
| subjects affected / exposed | 0 / 670 (0.00%) | 1 / 339 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 670 (0.00%) | 2 / 339 (0.59%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastritis | | | |
| subjects affected / exposed | 1 / 670 (0.15%) | 0 / 339 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 6 / 670 (0.90%) | 1 / 339 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 1 / 670 (0.15%) | 1 / 339 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inguinal hernia | | | |
| subjects affected / exposed | 0 / 670 (0.00%) | 2 / 339 (0.59%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal haemorrhage | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 670 (0.15%) | 0 / 339 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Apnoea | | | |
| subjects affected / exposed | 1 / 670 (0.15%) | 0 / 339 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchial obstruction | | | |
| subjects affected / exposed | 1 / 670 (0.15%) | 0 / 339 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cough | | | |
| subjects affected / exposed | 0 / 670 (0.00%) | 1 / 339 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea | | | |
| subjects affected / exposed | 0 / 670 (0.00%) | 1 / 339 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Nephrolithiasis | | | |
| subjects affected / exposed | 0 / 670 (0.00%) | 1 / 339 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Bronchiolitis | | | |
| subjects affected / exposed | 3 / 670 (0.45%) | 4 / 339 (1.18%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchitis | | | |
| subjects affected / exposed | 4 / 670 (0.60%) | 2 / 339 (0.59%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|---|---|---|
| Bronchopneumonia | | | |
| subjects affected / exposed | 4 / 670 (0.60%) | 1 / 339 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dacryocystitis | | | |
| subjects affected / exposed | 1 / 670 (0.15%) | 0 / 339 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis adenovirus | | | |
| subjects affected / exposed | 0 / 670 (0.00%) | 1 / 339 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis rotavirus | | | |
| subjects affected / exposed | 0 / 670 (0.00%) | 1 / 339 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Otitis media acute | | | |
| subjects affected / exposed | 0 / 670 (0.00%) | 1 / 339 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Periorbital cellulitis | | | |
| subjects affected / exposed | 1 / 670 (0.15%) | 0 / 339 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pertussis | | | |
| subjects affected / exposed | 1 / 670 (0.15%) | 0 / 339 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 4 / 670 (0.60%) | 2 / 339 (0.59%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia bacterial | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 670 (0.00%) | 1 / 339 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis acute | | | |
| subjects affected / exposed | 2 / 670 (0.30%) | 0 / 339 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory syncytial virus bronchiolitis | | | |
| subjects affected / exposed | 2 / 670 (0.30%) | 3 / 339 (0.88%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 670 (0.00%) | 1 / 339 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 1 / 670 (0.15%) | 0 / 339 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 670 (0.15%) | 0 / 339 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 1 / 670 (0.15%) | 0 / 339 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 670 (0.00%) | 1 / 339 (0.29%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypernatraemia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 670 (0.15%) | 0 / 339 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| **Non-serious adverse events** | Rotarix Group | Placebo Group | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 133 / 670 (19.85%) | 66 / 339 (19.47%) | |
| General disorders and administration site conditions | | | |
| Fever | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[1] | 54 / 203 (26.60%) | 29 / 100 (29.00%) | |
| occurrences (all) | 54 | 29 | |
| Irritability | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[2] | 133 / 203 (65.52%) | 66 / 100 (66.00%) | |
| occurrences (all) | 133 | 66 | |
| Pyrexia | | | |
| subjects affected / exposed[3] | 28 / 203 (13.79%) | 25 / 100 (25.00%) | |
| occurrences (all) | 28 | 25 | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[4] | 9 / 203 (4.43%) | 5 / 100 (5.00%) | |
| occurrences (all) | 9 | 5 | |
| Vomiting | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[5] | 52 / 203 (25.62%) | 27 / 100 (27.00%) | |
| occurrences (all) | 52 | 27 | |
| Metabolism and nutrition disorders | | | |
| Loss of appetite | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed[6] | 81 / 203 (39.90%) | 45 / 100 (45.00%) | |
| occurrences (all) | 81 | 45 | |

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The number of subjects exposed to the adverse event may differ from the total number of subjects exposed for the reporting group as subjects who missed reporting symptoms were treated as subjects without symptoms.
[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The number of subjects exposed to the adverse event may differ from the total number of subjects exposed for the reporting group as subjects who missed reporting symptoms were treated as subjects without symptoms.
[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The number of subjects exposed to the adverse event may differ from the total number of subjects exposed for the reporting group as subjects who missed reporting symptoms were treated as subjects without symptoms.
[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The number of subjects exposed to the adverse event may differ from the total number of subjects exposed for the reporting group as subjects who missed reporting symptoms were treated as subjects without symptoms.
[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The number of subjects exposed to the adverse event may differ from the total number of subjects exposed for the reporting group as subjects who missed reporting symptoms were treated as subjects without symptoms.
[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: The number of subjects exposed to the adverse event may differ from the total number of subjects exposed for the reporting group as subjects who missed reporting symptoms were treated as subjects without symptoms.

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 11 June 2007 | Amendment 3<br>The present study will be conducted to evaluate the safety, reactogenicity and immunogenicity of the HRV vaccine when used in pre-term infants aged between 6 and 14 weeks at the time of first dose in Portugal, France and Poland and in preterm infants aged between 6 and 12 weeks at the time of first dose in Spain. The study will be performed in four European countries (France, Poland, Portugal and Spain).<br>(Amendment 3:11 June 2007) |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported