Clinical trial results:
A phase III, double-blind, randomised, placebo-controlled, multi-centre study in Japan to assess the efficacy, safety, reactogenicity and immunogenicity of the lyophilised formulation of GlaxoSmithKline (GSK) Biologicals' live attenuated human rotavirus (HRV) vaccine, given as a two-dose primary vaccination course, in healthy infants previously uninfected with HRV.

Summary

EudraCT number	2015-001543-36
Trial protocol	Outside EU/EEA
Global end of trial date	21 November 2009

Results information

Result version number	v2 (current)
This version publication date	03 April 2021
First version publication date	18 July 2015
Version creation reason	• Correction of full data set Minor corrections in safety section.

Trial information

Trial identification

Sponsor protocol code	107625

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00480324
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:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	23 March 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 March 2009
Global end of trial reached?	Yes
Global end of trial date	21 November 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine if two doses of the lyophilised formulation of GSK Biologicals' HRV vaccine can prevent any RV GE leading to a medical intervention and caused by the circulating wild-type RV strains during the efficacy follow-up period.

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 the HRV vaccine/placebo.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	19 June 2007
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy, Ethical reason
Long term follow-up duration	17 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Japan: 765
Worldwide total number of subjects	765
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	765
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: -

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 Period (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Blinding implementation details:

The parents/guardians of the subjects, the study personnel and the investigator were unaware of the study vaccine administered (HRV vaccine or placebo). Blinding was maintained for the whole study period.

Arms

Are arms mutually exclusive?	Yes
Arm title	Rotarix Group

Arm description:

Subjects received 2 oral doses of Rotarix according to a 0, 1 month schedule.

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:

Two-dose oral vaccination.

Arm title	Placebo Group

Arm description:

Subjects received 2 oral doses of placebo according to a 0, 1 month schedule.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for 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	508	257
Completed	476	241
Not completed	32	16
Consent withdrawn by subject	14	5
Adverse event, non-fatal	1	1
Protocol Violation	-	1
Lost to follow-up	17	8
Subject’s mother pregnant	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Rotarix Group
Reporting group description:	
Subjects received 2 oral doses of Rotarix according to a 0, 1 month schedule.	
Reporting group title	Placebo Group
Reporting group description:	
Subjects received 2 oral doses of placebo according to a 0, 1 month schedule.	

Reporting group values	Rotarix Group	Placebo Group	Total
Number of subjects	508	257	765
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			
arithmetic mean	7.7	7.7	
standard deviation	± 1.99	± 2.05	-
Gender categorical			
Units: Subjects			
Female	229	134	363
Male	279	123	402

End points

End points reporting groups

Reporting group title	Rotarix Group
Reporting group description:	
Subjects received 2 oral doses of Rotarix according to a 0, 1 month schedule.	
Reporting group title	Placebo Group
Reporting group description:	
Subjects received 2 oral doses of placebo according to a 0, 1 month schedule.	

Primary: Number of subjects reporting any rotavirus (RV) gastroenteritis (GE) leading to medical intervention and caused by the circulating wild-type RV strains

End point title	Number of subjects reporting any rotavirus (RV) gastroenteritis (GE) leading to medical intervention and caused by the circulating wild-type RV strains[1]
End point description:	
Rotavirus (RV) gastroenteritis (GE) was defined as an episode of any severity GE leading to a medical intervention occurring at least two weeks after dose 2 in which rotavirus other than vaccine strain is identified in a stool sample collected as soon as possible but preferably not later than 7 days after the start of the episode.	
End point type	Primary
End point timeframe:	
From 2 weeks after Dose 2 up to 2 years of age	

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	498	250		
Units: Subjects	14	34		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting severe rotavirus (RV) gastroenteritis (GE) leading to medical intervention and caused by the circulating wild-type RV strains

End point title	Number of subjects reporting severe rotavirus (RV) gastroenteritis (GE) leading to medical intervention and caused by the circulating wild-type RV strains
End point description:	
A subject was considered as reporting severe rotavirus gastroenteritis when the subject scored 11 or more on a 20-point scoring system (Vesikari scoring system).	
End point type	Secondary
End point timeframe:	
From 2 weeks after Dose 2 up to 2 years of age	

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	498	250		
Units: Subjects	2	12		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any rotavirus (RV) gastroenteritis (GE) and severe RV GE leading to medical intervention and caused by the circulating wild-type RV strains of G1 type

End point title	Number of subjects reporting any rotavirus (RV) gastroenteritis (GE) and severe RV GE leading to medical intervention and caused by the circulating wild-type RV strains of G1 type

End point description:

Rotavirus (RV) gastroenteritis (GE) was defined as an episode of any severity GE leading to a medical intervention occurring at least two weeks after dose 2 in which rotavirus other than vaccine strain is identified in a stool sample collected as soon as possible but preferably not later than 7 days after the start of the episode. Severe RV GE was defined as an episode of rotavirus gastroenteritis with score ≥ 11 on a 20-point scoring system (Vesikari scoring system).

End point type	Secondary

End point timeframe:

From 2 weeks after Dose 2 up to 2 years of age

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	498	250		
Units: Subjects				
Any RV GE	4	13		
Severe RV GE	1	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any rotavirus (RV) gastroenteritis (GE) and severe RV GE leading to medical intervention and caused by the circulating wild-type RV strains of non-G1 types

End point title	Number of subjects reporting any rotavirus (RV) gastroenteritis (GE) and severe RV GE leading to medical intervention and caused by the circulating wild-type RV strains of non-G1 types

End point description:

Rotavirus (RV) gastroenteritis (GE) was defined as an episode of any severity GE leading to a medical intervention occurring at least two weeks after dose 2 in which rotavirus other than vaccine strain is identified in a stool sample collected as soon as possible but preferably not later than 7 days after the start of the episode. Severe rotavirus gastroenteritis was defined as an episode of rotavirus gastroenteritis with score ≥ 11 on a 20-point scoring system (Vesikari scoring system).

End point type	Secondary

End point timeframe:

From 2 weeks after Dose 2 up to 2 years of age

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	498	250		
Units: Subjects				
Any RV GE	10	21		
Severe RV GE	1	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects hospitalized due to rotavirus (RV) gastroenteritis (GE) caused by the circulating wild-type RV strains

End point title	Number of subjects hospitalized due to rotavirus (RV) gastroenteritis (GE) caused by the circulating wild-type RV strains

End point description:

Rotavirus (RV) gastroenteritis (GE) was defined as an episode of any severity GE leading to a medical intervention occurring at least two weeks after dose 2 in which rotavirus other than vaccine strain is identified in a stool sample collected as soon as possible but preferably not later than 7 days after the start of the episode.

End point type	Secondary

End point timeframe:

From 2 weeks after Dose 2 up to 2 years of age

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	498	250		
Units: Subjects	1	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any rotavirus (RV) gatroenteritis (GE) and severe RV GE leading to medical intervention and caused by the circulating wild-type RV strains

End point title	Number of subjects reporting any rotavirus (RV) gatroenteritis (GE) and severe RV GE leading to medical intervention and caused by the circulating wild-type RV strains

End point description:

Rotavirus (RV) gastroenteritis (GE) was defined as an episode of any severity GE leading to a medical intervention occurring at least two weeks after dose 2 in which rotavirus other than vaccine strain is identified in a stool sample collected as soon as possible but preferably not later than 7 days after the start of the episode. Severe rotavirus gastroenteritis was defined as an episode of rotavirus gastroenteritis with score ≥ 11 on a 20-point scoring system (Vesikari scoring system).

End point type	Secondary

End point timeframe:

From Dose 1 up to 2 years of age

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	508	257		
Units: Subjects				
Any RV GE	14	36		
Severe RV GE	2	13		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum anti-rotavirus immunoglobulin A (IgA) antibody concentration

End point title	Serum anti-rotavirus immunoglobulin A (IgA) antibody concentration

End point description:

Anti-rotavirus immunoglobulin A antibody concentrations are given as geometric mean concentrations (GMCs). Arbitrary 'zero' values were set in the Placebo Group since the GMC was below the assay cut-off value (20 U/mL).

End point type	Secondary

End point timeframe:

2 months after Dose 2

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	20		
Units: U/mL				
geometric mean (confidence interval 95%)	217 (109.9 to 428.6)	0 (0 to 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroconverted for anti-rotavirus immunoglobulin A (IgA) antibodies

End point title	Number of subjects seroconverted for anti-rotavirus immunoglobulin A (IgA) antibodies

End point description:

Seroconversion was defined as the appearance of anti-rotavirus immunoglobulin A antibody concentration ≥ 20 units (U)/milliliter (mL) in subjects initially (i.e. prior to the first dose of rotarix) seronegative.

End point type	Secondary

End point timeframe:

2 months after Dose 2

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	34	20		
Units: Subjects	29	1		

Statistical analyses

No statistical analyses for this end point

Secondary: 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

End point description:

Solicited general symptoms assessed were cough, diarrhoea, fever, irritability, loss of appetite and vomiting. Any = any solicited general symptom irrespective of intensity grade or relationship to vaccination. Grade 3 Cough/runny nose = cough/runny nose which prevented daily activity, Grade 3 Diarrhoea = ≥ 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 Vomiting = ≥ 3 episodes of vomiting/day and Grade 3 fever = Temperature axillary > 39.0°C. Related = general symptom assessed by the investigator as causally related to the study vaccination.

End point type	Secondary

End point timeframe:

During the 8-day follow-up period after each dose and overall.

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	508	257		
Units: Subjects				
Cough	184	92		
Diarrhoea	43	14		
Fever	62	22		
Irritability	261	125		
Loss of appetite	81	33		
Vomiting	74	36		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited adverse events (AEs)

End point title	Number of subjects reporting any unsolicited adverse events (AEs)

End point description:

Unsolicited adverse event (AE) was defined as any untoward medical occurrence in a patient or 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:

During the 31-day follow-up period after each dose

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	508	257		
Units: Subjects				
any AE (s)	279	144		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting serious adverse events (SAEs)

End point title	Number of subjects reporting serious adverse events (SAEs)

End point description:

Serious adverse events (SAEs) assessed include medical occurrences that result in death, are life

threatening, require hospitalization or prolongation of hospitalization, result in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subject.

End point type	Secondary

End point timeframe:

Up to 2 years of age

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	508	257		
Units: Subjects	72	44		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms during the 8-day (Day 0-7) solicited follow-up period after each dose of HRV vaccine/Placebo, Unsolicited AEs during the 31 days (Day 0-30) after any dose of HRV vaccine/Placebo and SAEs during the entire period (Dose1 up to Visit 5).

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	12.1

Reporting groups

Reporting group title	Placebo Group

Reporting group description:

Subjects received 2 oral doses of placebo according to a 0, 1 month schedule.

Reporting group title	Rotarix Group

Reporting group description:

Subjects received 2 oral doses of Rotarix according to a 0, 1 month schedule.

Serious adverse events	Placebo Group	Rotarix Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	44 / 257 (17.12%)	72 / 508 (14.17%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Fibroma			
subjects affected / exposed	0 / 257 (0.00%)	1 / 508 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasm			
subjects affected / exposed	0 / 257 (0.00%)	1 / 508 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Teratoma			

subjects affected / exposed	0 / 257 (0.00%)	1 / 508 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Kawasaki's disease			
subjects affected / exposed	1 / 257 (0.39%)	1 / 508 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 257 (0.39%)	3 / 508 (0.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	3 / 257 (1.17%)	5 / 508 (0.98%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenoidal hypertrophy			
subjects affected / exposed	1 / 257 (0.39%)	0 / 508 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhinorrhoea			
subjects affected / exposed	0 / 257 (0.00%)	1 / 508 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract inflammation			
subjects affected / exposed	1 / 257 (0.39%)	0 / 508 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Breath holding			

subjects affected / exposed	1 / 257 (0.39%)	0 / 508 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 257 (0.39%)	0 / 508 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skull fracture			
subjects affected / exposed	1 / 257 (0.39%)	0 / 508 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	0 / 257 (0.00%)	1 / 508 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Cryptorchism			
subjects affected / exposed	1 / 257 (0.39%)	0 / 508 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	1 / 257 (0.39%)	4 / 508 (0.79%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Convulsion			
subjects affected / exposed	2 / 257 (0.78%)	1 / 508 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status epilepticus			

subjects affected / exposed	1 / 257 (0.39%)	0 / 508 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 257 (0.39%)	0 / 508 (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			
Iron deficiency anaemia			
subjects affected / exposed	2 / 257 (0.78%)	1 / 508 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aplasia pure red cell			
subjects affected / exposed	1 / 257 (0.39%)	0 / 508 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Conjunctivitis			
subjects affected / exposed	0 / 257 (0.00%)	1 / 508 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Enterocolitis			
subjects affected / exposed	1 / 257 (0.39%)	2 / 508 (0.39%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorder			
subjects affected / exposed	2 / 257 (0.78%)	1 / 508 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematochezia			
subjects affected / exposed	0 / 257 (0.00%)	2 / 508 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Colitis			
subjects affected / exposed	0 / 257 (0.00%)	1 / 508 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	0 / 257 (0.00%)	1 / 508 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	0 / 257 (0.00%)	1 / 508 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	0 / 257 (0.00%)	1 / 508 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	2 / 257 (0.78%)	0 / 508 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			
subjects affected / exposed	0 / 257 (0.00%)	1 / 508 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	1 / 257 (0.39%)	0 / 508 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			

subjects affected / exposed	4 / 257 (1.56%)	12 / 508 (2.36%)	
occurrences causally related to treatment / all	0 / 4	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 257 (0.00%)	14 / 508 (2.76%)	
occurrences causally related to treatment / all	0 / 0	0 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	2 / 257 (0.78%)	11 / 508 (2.17%)	
occurrences causally related to treatment / all	0 / 2	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
subjects affected / exposed	3 / 257 (1.17%)	5 / 508 (0.98%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	2 / 257 (0.78%)	6 / 508 (1.18%)	
occurrences causally related to treatment / all	0 / 2	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	3 / 257 (1.17%)	5 / 508 (0.98%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Exanthema subitum			
subjects affected / exposed	2 / 257 (0.78%)	3 / 508 (0.59%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 257 (0.39%)	4 / 508 (0.79%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			

subjects affected / exposed	2 / 257 (0.78%)	2 / 508 (0.39%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media acute			
subjects affected / exposed	3 / 257 (1.17%)	1 / 508 (0.20%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	2 / 257 (0.78%)	2 / 508 (0.39%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis rotavirus			
subjects affected / exposed	2 / 257 (0.78%)	1 / 508 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	2 / 257 (0.78%)	1 / 508 (0.20%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute tonsilitis			
subjects affected / exposed	1 / 257 (0.39%)	1 / 508 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenovirus infection			
subjects affected / exposed	2 / 257 (0.78%)	0 / 508 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	2 / 257 (0.78%)	0 / 508 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis viral			

subjects affected / exposed	0 / 257 (0.00%)	2 / 508 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	1 / 257 (0.39%)	1 / 508 (0.20%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngitis			
subjects affected / exposed	0 / 257 (0.00%)	2 / 508 (0.39%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	1 / 257 (0.39%)	0 / 508 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial infection			
subjects affected / exposed	0 / 257 (0.00%)	1 / 508 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erythema infectiosum			
subjects affected / exposed	1 / 257 (0.39%)	0 / 508 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasopharyngitis			
subjects affected / exposed	1 / 257 (0.39%)	0 / 508 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
subjects affected / exposed	0 / 257 (0.00%)	1 / 508 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pertussis			

subjects affected / exposed	1 / 257 (0.39%)	0 / 508 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia respiratory syncytial viral			
subjects affected / exposed	0 / 257 (0.00%)	1 / 508 (0.20%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			
subjects affected / exposed	1 / 257 (0.39%)	0 / 508 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	1 / 257 (0.39%)	0 / 508 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	1 / 257 (0.39%)	0 / 508 (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 / 257 (0.39%)	3 / 508 (0.59%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight gain poor			
subjects affected / exposed	1 / 257 (0.39%)	0 / 508 (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	Placebo Group	Rotarix Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	204 / 257 (79.38%)	411 / 508 (80.91%)	
General disorders and administration site conditions			
Cough			
alternative assessment type: Systematic			
subjects affected / exposed	92 / 257 (35.80%)	184 / 508 (36.22%)	
occurrences (all)	92	184	
Diarrhoea			
alternative assessment type: Systematic			
subjects affected / exposed	14 / 257 (5.45%)	43 / 508 (8.46%)	
occurrences (all)	14	43	
Fever			
alternative assessment type: Systematic			
subjects affected / exposed	22 / 257 (8.56%)	62 / 508 (12.20%)	
occurrences (all)	22	62	
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed	125 / 257 (48.64%)	261 / 508 (51.38%)	
occurrences (all)	125	261	
Loss of appetite			
alternative assessment type: Systematic			
subjects affected / exposed	33 / 257 (12.84%)	81 / 508 (15.94%)	
occurrences (all)	33	81	
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed	36 / 257 (14.01%)	74 / 508 (14.57%)	
occurrences (all)	36	74	
Respiratory, thoracic and mediastinal disorders			
Upper respiratory tract inflammation			
subjects affected / exposed	16 / 257 (6.23%)	33 / 508 (6.50%)	
occurrences (all)	16	33	
Rhinorrhoea			
subjects affected / exposed	21 / 257 (8.17%)	19 / 508 (3.74%)	
occurrences (all)	21	19	

Skin and subcutaneous tissue disorders Eczema subjects affected / exposed occurrences (all)	 29 / 257 (11.28%) 29	 72 / 508 (14.17%) 72	
Infections and infestations Upper respiratory tract infection subjects affected / exposed occurrences (all) Nasopharyngitis subjects affected / exposed occurrences (all)	 25 / 257 (9.73%) 25 13 / 257 (5.06%) 13	 50 / 508 (9.84%) 50 31 / 508 (6.10%) 31	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 May 2007	The protocol has been amended as per the request from Pharmaceutical and Medical Devices Agency (PMDA), Japan.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported