Clinical trial results:
A phase III, double-blind, randomised, placebo-controlled, multi-centre study to assess the efficacy, immunogenicity and safety of two doses of GSK Biologicals' oral live attenuated liquid human rotavirus (HRV) vaccine in healthy Chinese infants.

Summary

EudraCT number	2012-005200-18
Trial protocol	Outside EU/EEA
Global end of trial date	12 May 2012

Results information

Result version number	v1
This version publication date	18 April 2016
First version publication date	11 June 2015

Trial information

Trial identification

Sponsor protocol code	113808

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01171963
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 Disclosure Advisor, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Disclosure Advisor, 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	12 May 2012
Is this the analysis of the primary completion data?	Yes
Primary completion date	12 May 2012
Global end of trial reached?	Yes
Global end of trial date	12 May 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of two doses of GSK Biologicals' liquid HRV vaccine against severe RV GE caused by the circulating wild-type RV strains during the efficacy follow-up period.
Criteria: The primary objective will be reached if the lower limit of the 95% Confidence Interval (CI) on vaccine efficacy is at least 10%

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 vaccines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 August 2010
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	China: 3340
Worldwide total number of subjects	3340
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)	3340
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:

Duration of the study was of a maximum of 21 months, with the enrolment of subjects starting in August 2010, and subjects being followed up to May 2012 (study Month 21 and Study End), end of the rotavirus season in China.

Pre-assignment

Screening details:

Subjects were assigned to 2 sub-cohorts (1:1 ratio). Sub-cohort 1 and Sub-cohort 2 subjects received their OPV and Infanrix™ EPI vaccination respectively independently of, and concomitantly with their Rotarix™/placebo vaccination. 3340 subjects were allocated study subject number allocated and 3333 subjects were vaccinated.

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
Arm title	Rotarix Group

Arm description:

Subjects aged between and including 6 and 16 weeks at the time of first vaccination received 2 doses of Rotarix™ vaccine, liquid formulation, at Day 0 and at Month 1. As part of the routine childhood vaccination according to the Expanded Program of Immunization (EPI) recommendations in China, subjects in this group also received 3 doses of Infanrix™ vaccine and 3 doses of the oral poliovirus vaccine manufactured by the Institute of Medical Biology of the Chinese Academy of Medical Sciences (OPV). The Infanrix™ and the OPV vaccines were administered independently of (Sub-cohort 1) or concomitantly with (Sub-cohort 2) the Rotarix™ vaccine. When administered concomitantly, subjects received the 3 doses of Infanrix™ vaccine at Months 1, 2 and 3, and the 3 doses of the OPV vaccine at Day 0, Month 1 and Month 2. The Rotarix™ and OPV vaccines were administered orally; the Infanrix™ vaccine was administered intramuscularly in the left anterolateral thigh.

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 doses administered orally.

Investigational medicinal product name	Infanrix™
Investigational medicinal product code	
Other name	DTPa
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses administered intramuscularly in the left anterolateral thigh.

Investigational medicinal product name	Oral poliovirus vaccine (OPV)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral liquid
Routes of administration	Oral use

Dosage and administration details:

3 doses administered orally.

Arm title	Placebo Group

Arm description:

Subjects aged between and including 6 and 16 weeks at the time of first vaccination received 2 doses of Placebo at Day 0 and at Month 1. As part of the routine childhood vaccination according to the Expanded Program of Immunization (EPI) recommendations in China, subjects in this group also received 3 doses of Infanrix™ vaccine and 3 doses of the oral poliovirus vaccine manufactured by the Institute of Medical Biology of the Chinese Academy of Medical Sciences (OPV). The Infanrix™ and the OPV vaccine were administered independently of (Sub-cohort 1) or concomitantly with (Sub-cohort 2) the Placebo. When administered concomitantly, subjects received the 3 doses of Infanrix™ vaccine at Months 1, 2 and 3, and the 3 doses of the OPV vaccine at Day 0, Month 1 and Month 2. The Placebo and the OPV vaccine were administered orally; the Infanrix™ vaccine was administered intramuscularly in the left anterolateral thigh.

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

Dosage and administration details:

Subjects received 2 doses of placebo at Day 0 and at Month 1, administered orally.

Investigational medicinal product name	Infanrix™
Investigational medicinal product code	
Other name	DTPa
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

3 doses administered intramuscularly in the left anterolateral thigh.

Investigational medicinal product name	Oral poliovirus vaccine (OPV)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral liquid
Routes of administration	Oral use

Dosage and administration details:

3 doses administered orally

Number of subjects in period 1[1]	Rotarix Group	Placebo Group
Started	1666	1667
Completed	1518	1499
Not completed	148	168
Adverse event, serious fatal	6	7
Consent withdrawn by subject	55	46
Adverse event, non-fatal	4	8

Not willing to participate in the EFU-visit 7	59	83
Migrated/moved from study area	23	24
Diarrhea	1	-

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: 3340 subjects were allocated study subject number allocated and 3333 subjects were vaccinated.

Baseline characteristics

Reporting groups	
Reporting group title	Rotarix Group

Reporting group description:

Subjects aged between and including 6 and 16 weeks at the time of first vaccination received 2 doses of Rotarix™ vaccine, liquid formulation, at Day 0 and at Month 1. As part of the routine childhood vaccination according to the Expanded Program of Immunization (EPI) recommendations in China, subjects in this group also received 3 doses of Infanrix™ vaccine and 3 doses of the oral poliovirus vaccine manufactured by the Institute of Medical Biology of the Chinese Academy of Medical Sciences (OPV). The Infanrix™ and the OPV vaccines were administered independently of (Sub-cohort 1) or concomitantly with (Sub-cohort 2) the Rotarix™ vaccine. When administered concomitantly, subjects received the 3 doses of Infanrix™ vaccine at Months 1, 2 and 3, and the 3 doses of the OPV vaccine at Day 0, Month 1 and Month 2. The Rotarix™ and OPV vaccines were administered orally; the Infanrix™ vaccine was administered intramuscularly in the left anterolateral thigh.

Reporting group title	Placebo Group

Reporting group description:

Subjects aged between and including 6 and 16 weeks at the time of first vaccination received 2 doses of Placebo at Day 0 and at Month 1. As part of the routine childhood vaccination according to the Expanded Program of Immunization (EPI) recommendations in China, subjects in this group also received 3 doses of Infanrix™ vaccine and 3 doses of the oral poliovirus vaccine manufactured by the Institute of Medical Biology of the Chinese Academy of Medical Sciences (OPV). The Infanrix™ and the OPV vaccine were administered independently of (Sub-cohort 1) or concomitantly with (Sub-cohort 2) the Placebo. When administered concomitantly, subjects received the 3 doses of Infanrix™ vaccine at Months 1, 2 and 3, and the 3 doses of the OPV vaccine at Day 0, Month 1 and Month 2. The Placebo and the OPV vaccine were administered orally; the Infanrix™ vaccine was administered intramuscularly in the left anterolateral thigh.

Reporting group values	Rotarix Group	Placebo Group	Total
Number of subjects	1666	1667	3333
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	9.5	9.7	
standard deviation	± 2.64	± 2.59	-
Gender categorical Units: Subjects			
Female	795	836	1631
Male	871	831	1702

End points

End points reporting groups

Reporting group title	Rotarix Group

Reporting group description:

Subjects aged between and including 6 and 16 weeks at the time of first vaccination received 2 doses of Rotarix™ vaccine, liquid formulation, at Day 0 and at Month 1. As part of the routine childhood vaccination according to the Expanded Program of Immunization (EPI) recommendations in China, subjects in this group also received 3 doses of Infanrix™ vaccine and 3 doses of the oral poliovirus vaccine manufactured by the Institute of Medical Biology of the Chinese Academy of Medical Sciences (OPV). The Infanrix™ and the OPV vaccines were administered independently of (Sub-cohort 1) or concomitantly with (Sub-cohort 2) the Rotarix™ vaccine. When administered concomitantly, subjects received the 3 doses of Infanrix™ vaccine at Months 1, 2 and 3, and the 3 doses of the OPV vaccine at Day 0, Month 1 and Month 2. The Rotarix™ and OPV vaccines were administered orally; the Infanrix™ vaccine was administered intramuscularly in the left anterolateral thigh.

Reporting group title	Placebo Group

Reporting group description:

Subjects aged between and including 6 and 16 weeks at the time of first vaccination received 2 doses of Placebo at Day 0 and at Month 1. As part of the routine childhood vaccination according to the Expanded Program of Immunization (EPI) recommendations in China, subjects in this group also received 3 doses of Infanrix™ vaccine and 3 doses of the oral poliovirus vaccine manufactured by the Institute of Medical Biology of the Chinese Academy of Medical Sciences (OPV). The Infanrix™ and the OPV vaccine were administered independently of (Sub-cohort 1) or concomitantly with (Sub-cohort 2) the Placebo. When administered concomitantly, subjects received the 3 doses of Infanrix™ vaccine at Months 1, 2 and 3, and the 3 doses of the OPV vaccine at Day 0, Month 1 and Month 2. The Placebo and the OPV vaccine were administered orally; the Infanrix™ vaccine was administered intramuscularly in the left anterolateral thigh.

Primary: Number of subjects with severe episode(s) of rotavirus gastroenteritis (RVGE) caused by the circulating wild type (WT) strains

End point title	Number of subjects with severe episode(s) of rotavirus gastroenteritis (RVGE) caused by the circulating wild type (WT) strains[1]

End point description:

A gastroenteritis episode was classified positive for rotavirus (RV) and caused by the circulating wild-type (WT) RV strains if RV other than the vaccine strain was identified in a stool sample collected during the episode. Severe RVGE was defined as an episode of RV GE with score equal to or higher than (>=) 11 on a 20-point Vesikari scoring system.

End point type	Primary

End point timeframe:

From Month 1 ½ to Month 21

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	1575	1573		
Units: Subjects				
Subjects with severe WT RVGE	21	75		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any episode(s) of rotavirus gastroenteritis (RVGE) caused by the circulating wild-type strains

End point title	Number of subjects with any episode(s) of rotavirus gastroenteritis (RVGE) caused by the circulating wild-type strains

End point description:

A gastroenteritis episode was classified positive for rotavirus (RV) and caused by the circulating wild-type (WT) RV strains if RV other than the vaccine strain was identified in a stool sample collected during the episode.

End point type	Secondary

End point timeframe:

From Month 1 ½ to Month 21

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1575	1573		
Units: Subjects				
Subjects with WT RVGE	70	167		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any episode(s) of rotavirus gastroenteritis (RVGE) of any type.

End point title	Number of subjects with any episode(s) of rotavirus gastroenteritis (RVGE) of any type.

End point description:

A gastroenteritis episode was classified positive for rotavirus (RV) if RV was identified in a stool sample collected during the episode. RV types assessed were G1 Wild Type (G1WT), G2, G3, G9, GX (G type unknown, but not vaccine strain), P4, P8 Wild Type (P8WT), P9, PX (P type unknown, but not vaccine strain) and Pooled Non-G1WT.

End point type	Secondary

End point timeframe:

From Month 1 ½ to Month 21

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1575	1573		
Units: Subjects				
Subjects with G1WT RVGE	22	46		
Subjects with G2 RVGE	42	105		
Subjects with G3 RVGE	1	12		
Subjects with G9 RVGE	1	5		
Subjects with GX RVGE	6	8		
Subjects with P4 RVGE	43	107		
Subjects with P8WT RVGE	25	59		
Subjects with P9 RVGE	0	1		
Subjects with PX RVGE	4	1		
Subjects with Pooled Non-G1WT RVGE	49	129		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with severe episode(s) of rotavirus gastroenteritis (RVGE) of any type

End point title	Number of subjects with severe episode(s) of rotavirus gastroenteritis (RVGE) of any type

End point description:

A gastroenteritis episode was classified positive for rotavirus (RV) if RV was identified in a stool sample collected during the episode. Severe RVGE was defined as an episode of RVGE with score equal to or higher than (>=) 11 on a 20-point Vesikari scoring system. RV types assessed were G1 Wild Type (G1WT), G2, G3, G9, GX (G type unknown, but not vaccine strain), P4, P8 Wild Type (P8WT), P9, PX (P type unknown, but not vaccine strain) and Pooled Non-G1WT.

End point type	Secondary

End point timeframe:

From Month 1 ½ to Month 21

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1575	1573		
Units: Subjects				
Subjects with severe G1WT RVGE	9	25		
Subjects with severe G2 RVGE	11	43		
Subjects with severe G3 RVGE	0	3		
Subjects with severe G9 RVGE	0	3		
Subjects with severe GX RVGE	1	6		
Subjects with severe P4 RVGE	12	43		
Subjects with severe P8WT RVGE	9	31		
Subjects with severe PX RVGE	1	1		
Subjects with severe Pooled Non-G1WT RVGE	12	54		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with episodes of rotavirus gastroenteritis (RVGE) caused by the circulating wild type (WT) strains requiring hospitalization

End point title	Number of subjects with episodes of rotavirus gastroenteritis (RVGE) caused by the circulating wild type (WT) strains requiring hospitalization

End point description:

A gastroenteritis episode was classified positive for rotavirus (RV) and caused by the circulating WT RV strains if RV other than the vaccine strain was identified in a stool sample collected during the episode.

End point type	Secondary

End point timeframe:

From Month 1 ½ to Month 21

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1575	1573		
Units: Subjects				
Subjects with RVGE requiring hospitalization	4	21		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any and severe gastroenteritis (GE) due to any cause

End point title	Number of subjects with any and severe gastroenteritis (GE) due to any cause

End point description:

Severe GE was defined as an episode of GE with score equal to or higher than (>=) 11 on a 20-point Vesikari scoring system. This outcome measure concerns results for GE episodes due to any cause.

End point type	Secondary

End point timeframe:

From Month 1 ½ to Month 21

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1575	1573		
Units: Subjects				
Subjects with any GE	728	759		
Subjects with any severe GE	187	206		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any solicited general symptoms following vaccination with the Rotarix™ vaccine/placebo

End point title	Number of subjects with any solicited general symptoms following vaccination with the Rotarix™ vaccine/placebo

End point description:

Assessed solicited general symptoms were fever,defined as axillary temperature (T) above or equal to [>=] 37.5 degrees Celsius [°C] (if GSK scale) or >= 37.1°C (if Chinese scale), fussiness/irritability, loss of appetite, cough/runny nose, diarrhea and vomiting. Any = any occurrence of the specified solicited general symptom regardless of the intensity grade or relationship to vaccination. This outcome measure was only assessed in subjects from Sub-cohort 1, who received the EPI vaccination independently of study vaccination with the Rotarix™ vaccine/placebo.

End point type	Secondary

End point timeframe:

Within the 8-day (Days 0–7) follow-up periods after any dose of Rotarix™ vaccine/placebo

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1513	1514		
Units: Subjects				
Any cough/runny nose	313	366		
Any diarrhoea	127	123		
Any Irritability/Fussiness	415	448		
Any Loss of appetite	253	250		
Any Fever – Chinese scale: Axillary T >= 37.1°C	302	313		
Any Fever – GSK scale: Axillary T >= 37.5°C	83	104		
Any Vomiting	213	232		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any solicited general symptoms following administration of the co-administered EPI vaccines

End point title	Number of subjects with any solicited general symptoms following administration of the co-administered EPI vaccines

End point description:

Solicited general symptoms assessed following administration of the co-administered EPI vaccines were drowsiness, gastrointestinal symptoms, fussiness/irritability, loss of appetite, and fever, defined as axillary temperature (T) above or equal to [>=] 37.5 degrees Celsius [°C] (if GSK scale) or >= 37.1°C (if Chinese scale). Any = any occurrence of the specified solicited general symptom regardless of the intensity grade or relationship to vaccination. This outcome measure was only assessed in subjects from Sub-cohort 2, who received the EPI vaccination concomitantly with study vaccination with the Rotarix™ vaccine/placebo.

End point type	Secondary

End point timeframe:

Within the 8-day (Days 0–7) follow-up periods following Doses 1 and 2 of the OPV vaccine and Dose 1 of the Infanrix™ vaccine

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	153	153		
Units: Subjects				
Any Drowsiness	44	38		
Any Gastrointestinal	43	38		
Any Irritability/Fussiness	56	52		
Any Loss of appetite	43	32		
Any Fever – Chinese scale: Axillary T >= 37.1°C	18	20		
Any Fever – GSK scale: Axillary T >= 37.5°C	6	7		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with any solicited local symptoms following Dose 2 of the Rotarix™ vaccine/placebo

End point title	Number of subjects with any solicited local symptoms following Dose 2 of the Rotarix™ vaccine/placebo

End point description:

Solicited local symptoms assessed following administration of the co-administered EPI vaccines were pain, swelling, and redness. Any = any occurrence of the specified solicited local symptom regardless of the intensity grade. This outcome measure was only assessed in subjects from Sub-cohort 2, who received the EPI vaccination concomitantly with study vaccination with the Rotarix™ vaccine/placebo.

End point type	Secondary

End point timeframe:

Within the 8-day (Days 0–7) follow-up periods following Dose 2 of the Rotarix™ vaccine/placebo

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	150	151		
Units: Subjects				
Any Pain	14	9		
Any Redness	20	13		
Any Swelling	13	6		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

An unsolicited AE is any adverse event (i.e. any untoward medical occurrence in a patient or clinical investigation subject, temporally associated with use of a medicinal product, whether or not considered related to the medicinal product) 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 = occurrence of an unsolicited AE regardless of the intensity grade or relationship to vaccination.

End point type	Secondary

End point timeframe:

Within the 31-day (Days 0–30) follow-up periods following any dose of the Rotarix™ vaccine or placebo

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1666	1667		
Units: Subjects				
Any unsolicited AE(s)	310	368		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

SAEs assessed include medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization, or result in disability/incapacity. Any = occurrence of an SAE regardless of the intensity grade or relationship to vaccination.

End point type	Secondary

End point timeframe:

Throughout the entire study period (from Day 0 to Study End at Month 21)

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1666	1667		
Units: Subjects				
Any SAE(s)	183	246		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted subjects for anti-rotavirus (anti-RV) immunoglobulin A (IgA) antibodies in Immunogenicity sub-cohort 1

End point title	Number of seroconverted subjects for anti-rotavirus (anti-RV) immunoglobulin A (IgA) antibodies in Immunogenicity sub-cohort 1

End point description:

A seroconverted subject was defined as a subject seronegative at baseline (Day 0) with the appearance of anti-RV IgA antibody concentration greater than or equal to (≥) 20 units per milliliter (U/mL) at the time point assessed. A seronegative subject was defined as a subject with anti-RV IgA antibody concentration lower than (<) 20 U/mL.

End point type	Secondary

End point timeframe:

At Month 2 and at 12 months of age

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	257	254		
Units: Subjects				
Anti-RV IgA - Month 2 [N=257;254]	192	9		
Anti-RV IgA – 12 months of age [N=246;252]	176	118		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted subjects for anti-rotavirus (anti-RV) immunoglobulin A (IgA) antibodies in Immunogenicity sub-cohort 2

End point title	Number of seroconverted subjects for anti-rotavirus (anti-RV) immunoglobulin A (IgA) antibodies in Immunogenicity sub-cohort 2

End point description:

A seroconverted subject was defined as a subject seronegative at baseline (Day 0) with the appearance of anti-RV IgA antibody concentration greater than or equal to (≥) 20 units per milliliter (U/mL) at the time point assessed. A seronegative subject was defined as a subject with anti-RV IgA antibody concentration lower than (<) 20 U/mL.

End point type	Secondary

End point timeframe:

At Month 2 and at 12 months of age

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	134	139		
Units: Subjects				
Anti-RV IgA - Month 2 [N=134;139]	86	13		
Anti-RV IgA – 12 months of age [N=124;133]	62	29		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

A seroconverted subject was defined as a subject seronegative at baseline (Day 0) with the appearance of anti-RV IgA antibody concentration greater than or equal to (≥) 20 units per milliliter (U/mL) at the time point assessed. A seronegative subject was defined as a subject with anti-RV IgA antibody concentration lower than (<) 20 U/mL.

End point type	Secondary

End point timeframe:

At Month 2 and at 12 months of age

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	391	393		
Units: Subjects				
Anti-RV IgA - Month 2 [N=391;393]	278	22		
Anti-RV IgA – 12 months of age [N=370;385]	238	147		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seropositive for anti-rotavirus (anti-RV) immunoglobulin A (IgA) antibodies in Immunogenicity sub-cohort 1

End point title	Number of subjects seropositive for anti-rotavirus (anti-RV) immunoglobulin A (IgA) antibodies in Immunogenicity sub-cohort 1

End point description:

A subject seropositive for anti-rotavirus (anti-RV) immunoglobulin A (IgA) antibodies was defined as a subject anti-RV IgA antibody concentration greater than or equal to (≥) the seropositivity cut-off of 20 units per milliliter (U/mL).

End point type	Secondary

End point timeframe:

At Day 0, Month 2 and at 12 months of age

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	257	254		
Units: Subjects				
Anti-RV IgA – Day 0 [N=257;254]	0	0		
Anti-RV IgA - Month 2 [N=257;254]	192	9		
Anti-RV IgA – 12 months of age [N=246;252]	176	118		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seropositive for anti-rotavirus (anti-RV) immunoglobulin A (IgA) antibodies in Immunogenicity sub-cohort 2

End point title	Number of subjects seropositive for anti-rotavirus (anti-RV) immunoglobulin A (IgA) antibodies in Immunogenicity sub-cohort 2

End point description:

A subject seropositive for anti-rotavirus (anti-RV) immunoglobulin A (IgA) antibodies was defined as a subject anti-RV IgA antibody concentration greater than or equal to (≥) the seropositivity cut-off of 20 units per milliliter (U/mL).

End point type	Secondary

End point timeframe:

At Day 0, Month 2 and at 12 months of age

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	134	139		
Units: Subjects				
Anti-RV IgA – Day 0 [N=134;139]	0	0		
Anti-RV IgA - Month 2 [N=134;139]	86	13		
Anti-RV IgA – 12 months of age [N=124;133]	62	29		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

A subject seropositive for anti-rotavirus (anti-RV) immunoglobulin A (IgA) antibodies was defined as a subject anti-RV IgA antibody concentration greater than or equal to (≥) the seropositivity cut-off of 20 units per milliliter (U/mL).

End point type	Secondary

End point timeframe:

At Day 0, Month 2 and at 12 months of age

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	391	393		
Units: Subjects				
Anti-RV IgA – Day 0 [N=391;393]	0	0		
Anti-RV IgA - Month 2 [N=391;393]	278	22		
Anti-RV IgA – 12 months of age [N=370;385]	238	147		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-rotavirus (anti-RV) immunoglobulin A (IgA) antibody concentrations in Immunogenicity sub-cohort 1

End point title	Anti-rotavirus (anti-RV) immunoglobulin A (IgA) antibody concentrations in Immunogenicity sub-cohort 1

End point description:

Concentrations were expressed as geometric mean concentrations (GMCs), in units per milliliter (U/mL). The cut-off of the assay was the seropositivity cut-off (≥ 20 U/mL). At Day 0 for Rotarix Group and Placebo Group and Month 2 for the Placebo Group, no subjects had an antibody concentration equal or

above to the cut-off (20 U/mL).

End point type	Secondary

End point timeframe:

At Day 0, Month 2 and at 12 months of age

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	257	254		
Units: U/mL				
geometric mean (confidence interval 95%)				
Anti-RV IgA – Day 0 [N=257;254]	0 (0 to 0)	0 (0 to 0)		
Anti-RV IgA - Month 2 [N=257;254]	90.2 (73.3 to 111.1)	0 (0 to 0)		
Anti-RV IgA – 12 months of age [N=246;252]	66.5 (54.6 to 81)	35.3 (29.3 to 42.5)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-rotavirus (anti-RV) immunoglobulin A (IgA) antibody concentrations in Immunogenicity sub-cohort 2.

End point title	Anti-rotavirus (anti-RV) immunoglobulin A (IgA) antibody concentrations in Immunogenicity sub-cohort 2.

End point description:

Concentrations were expressed as geometric mean concentrations (GMCs), in units per milliliter (U/mL). The cut-off of the assay was the seropositivity cut-off (≥ 20 U/mL). At Day 0 for the Rotarix Group and Placebo Group and Month 2 and 12 months of age for Placebo Group, no subjects had an antibody concentration equal or above to the cut-off (20 U/mL).

End point type	Secondary

End point timeframe:

At Day 0, Month 2 and at 12 months of age.

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	134	139		
Units: U/mL				
geometric mean (confidence interval 95%)				
Anti-RV IgA – Day 0 [N=134;139]	0 (0 to 0)	0 (0 to 0)		
Anti-RV IgA - Month 2 [N=134;139]	84 (58.9 to 119.8)	0 (0 to 0)		
Anti-RV IgA – 12 months of age [N=124;133]	31.3 (24.6 to 39.8)	0 (0 to 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-rotavirus (anti-RV) immunoglobulin A (IgA) antibody concentrations

End point title	Anti-rotavirus (anti-RV) immunoglobulin A (IgA) antibody concentrations

End point description:

Concentrations were expressed as geometric mean concentrations (GMCs), in units per milliliter (U/mL). The cut-off of the assay was the seropositivity cut-off (≥ 20 U/mL). At Day 0 for Rotarix Group and Placebo Group and at Month 2 for Placebo group, no subjects had an antibody concentration equal or above to the cut-off (20 U/mL).

End point type	Secondary

End point timeframe:

At Day 0, Month 2 and at 12 months of age

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	391	393		
Units: U/mL				
geometric mean (confidence interval 95%)				
Anti-RV IgA – Day 0 [N=391;393]	0 (0 to 0)	0 (0 to 0)		
Anti-RV IgA - Month 2 [N=391;393]	88 (73.4 to 105.6)	0 (0 to 0)		
Anti-RV IgA – 12 months of age [N=370;385]	51.6 (44.1 to 60.5)	27.4 (23.7 to 31.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroprotected against diphtheria and tetanus

End point title	Number of subjects seroprotected against diphtheria and tetanus

End point description:

A subject seroprotected against diphtheria/tetanus was defined as a subject with an anti-diphtheria (anti-D)/anti-tetanus (anti-T) antibody concentrations greater than or equal to (≥) 0.1 international units per milliliter (IU/mL). This outcome measure concerns solely subjects in Sub-cohort 2, who received the EPI vaccination concomitantly with study vaccination with the Rotarix™ vaccine/placebo

End point type	Secondary

End point timeframe:

At Day 0 and at Month 4

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	133	139		
Units: Subjects				
Anti-D at Day 0 [N=133;138]	1	1		
Anti-D at Month 4 [N=133;139]	133	139		
Anti-T at Day 0 [N=133;138]	0	1		
Anti-T at Month 4 [N=133;139]	133	139		

Statistical analyses

No statistical analyses for this end point

Secondary: Anti-Diphtheria (Anti-D) and anti-tetanus (anti-T) antibody concentrations

End point title	Anti-Diphtheria (Anti-D) and anti-tetanus (anti-T) antibody concentrations

End point description:

Concentrations were expressed as geometric mean concentrations (GMCs) in international unit per milliliter (IU/mL). The cut-off of the assay was the seroprotection cut-off assay (≥ 0.1 IU/mL). This outcome measure concerns solely subjects in Sub-cohort 2, who received the EPI vaccination concomitantly with study vaccination with the Rotarix™ vaccine/placebo.

End point type	Secondary

End point timeframe:

At Day 0 and at Month 4

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	133	139		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-D at Day 0 [N=133;138]	0.051 (0.049 to 0.052)	0.05 (0.05 to 0.051)		
Anti-D at Month 4 [N=133;139]	0.375 (0.326 to 0.432)	0.334 (0.308 to 0.363)		
Anti-T at Day 0 [N=133;138]	0.05 (0.05 to 0.05)	0.05 (0.05 to 0.1)		
Anti-T at Month 4 [N=133;139]	1.281 (1.253 to 1.309)	1.343 (1.215 to 1.486)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroprotected against poliovirus types 1, 2 and 3

End point title	Number of subjects seroprotected against poliovirus types 1, 2 and 3

End point description:

A subject seroprotected against poliovirus types 1, 2 and 3 was defined as a subject with anti-poliovirus type 1 (anti-polio 1)/anti-polio 2/anti-polio 3 antibody titer greater than or equal to (≥) 8 estimated doses 50% (ED50). This outcome measure concerns solely subjects in Sub-cohort 2, who received the EPI vaccination concomitantly with study vaccination with the Rotarix™ vaccine/placebo (cf. population definition below).

End point type	Secondary

End point timeframe:

At Day 0 and at Month 4

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	139		
Units: Subjects				
Anti-polio 1 at Day 0	63	62		
Anti-polio 1 at Month 4	136	139		
Anti-polio 2 at Day 0	52	39		
Anti-polio 2 at Month 4	136	139		
Anti-polio 3 at Day 0	32	29		
Anti-polio 3 at Month 4	135	138		

Statistical analyses

No statistical analyses for this end point

Secondary: Titers for anti-poliovirus type 1 (anti-polio 1), anti-polio 2 and anti-polio 3 antibodies

End point title	Titers for anti-poliovirus type 1 (anti-polio 1), anti-polio 2 and anti-polio 3 antibodies

End point description:

Titers were expressed as geometric mean titers (GMTs). The cut-off of the assay was the seroprotection cut-off (≥ 8 estimated doses 50% [ED50] for anti-poliovirus type 1 [anti-polio 1]/anti-polio 2/anti-polio 3 antibodies. This outcome measure concerns solely subjects in Sub-cohort 2, who received the EPI vaccination concomitantly with study vaccination with the Rotarix™ vaccine/placebo.

End point type	Secondary

End point timeframe:

At Day 0 and at Month 4

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	136	139		
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-polio 1 at Day 0	8.9 (7.5 to 10.5)	9.1 (7.6 to 11)		
Anti-polio 1 at Month 4	2101.1 (1734.8 to 2544.8)	2259.4 (1844.4 to 2767.9)		
Anti-polio 2 at Day 0	7.6 (6.5 to 9)	6.2 (5.4 to 7.1)		
Anti-polio 2 at Month 4	402.5 (334.8 to 483.9)	425.1 (371 to 487.1)		
Anti-polio 3 at Day 0	5.6 (4.9 to 6.3)	5.7 (4.9 to 6.6)		
Anti-polio 3 at Month 4	426.6 (342.7 to 531)	360.3 (303 to 428.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seropositive for anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibodies

End point title	Number of subjects seropositive for anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin (anti-FHA) and anti-pertactin (anti-PRN) antibodies

End point description:

Antibody assessment was performed by enzyme-linked immunosorbent assay (ELISA). A subject seropositive for anti-PT/anti-FHA/anti-PRN antibodies was defined as a subject with an anti-PT/anti-FHA/anti-PRN antibody concentrations greater than or equal to (≥) 5 ELISA units per milliliter (EL.U/mL). This outcome measure concerns solely subjects in Sub-cohort 2, who received the EPI vaccination concomitantly with study vaccination with the Rotarix™ vaccine/placebo.

End point type	Secondary

End point timeframe:

At Day 0 and at Month 4

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	133	139		
Units: Subjects				
Anti-PT at Day 0 [N=131;139]	43	34		
Anti-PT at Month 4 [N=133;139]	133	139		
Anti-FHA at Day 0 [N=131;139]	31	47		

Anti-FHA at Month 4 [N=133;139]	133	139		
Anti-PRN at Day 0 [N=131;139]	3	5		
Anti-PRN at Month 4 [N=133;139]	133	139		

Statistical analyses

No statistical analyses for this end point

Secondary: Concentrations for anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin

End point title	Concentrations for anti-pertussis toxoid (anti-PT), anti-filamentous haemagglutinin

End point description:

Antibody assessment was performed by enzyme-linked immunosorbent assay (ELISA). Concentrations were expressed as geometric mean concentrations (GMCs) in ELISA units per milliliter (EL.U/mL). The cut-off of the assay was the seropositivity cut-off (≥ 5 EL.U/mL) for all antibodies assessed (anti-PT, anti-FHA and anti-PRN). This outcome measure concerns solely subjects in Sub-cohort 2, who received the EPI vaccination concomitantly with study vaccination with the Rotarix™ vaccine/placebo.

End point type	Secondary

End point timeframe:

At Day 0 and at Month 4

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	133	139		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-PT at Day 0 [N=131;139]	3.4 (3.1 to 3.7)	3.2 (3 to 3.4)		
Anti-PT at Month 4 [N=133;139]	88.9 (84.9 to 93.2)	90.5 (86.4 to 94.8)		
Anti-FHA at Day 0 [N=131;139]	3.1 (2.9 to 3.3)	3.5 (3.2 to 3.8)		
Anti-FHA at Month 4 [N=133;139]	59.5 (55.8 to 63.5)	65.8 (61.3 to 70.5)		
Anti-PRN at Month 0 [N=133;139]	2.6 (2.5 to 2.6)	2.6 (2.5 to 2.7)		
Anti-PRN at Month 4 [N=133;139]	41.9 (37.6 to 46.5)	50.8 (44.3 to 58.1)		

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. SAEs were collected throughout the entire study period (Months 0 to 21).

Adverse event reporting additional description:

1 subject in the Placebo Group experienced an SAE assessed by the investigators as causally related to study vaccination (Diarrhoea).
The number of occurrences reported for solicited symptoms, adverse events & SAEs 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	14.1

Reporting groups

Reporting group title	Rotarix Group
Reporting group description: -	
Reporting group title	Placebo Group

Reporting group description: -

Serious adverse events	Rotarix Group	Placebo Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	183 / 1666 (10.98%)	246 / 1667 (14.76%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute lymphocytic leukaemia			
subjects affected / exposed	0 / 1666 (0.00%)	1 / 1667 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Histiocytosis haematophagic			
subjects affected / exposed	0 / 1666 (0.00%)	1 / 1667 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
General disorders and administration site conditions			
Multi-organ failure			

subjects affected / exposed	1 / 1666 (0.06%)	2 / 1667 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 2	
Death			
subjects affected / exposed	0 / 1666 (0.00%)	1 / 1667 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Drowning			
subjects affected / exposed	1 / 1666 (0.06%)	0 / 1667 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hernia			
subjects affected / exposed	0 / 1666 (0.00%)	1 / 1667 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asphyxia			
subjects affected / exposed	2 / 1666 (0.12%)	0 / 1667 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 1666 (0.00%)	1 / 1667 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Asthma			
subjects affected / exposed	3 / 1666 (0.18%)	1 / 1667 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Brain contusion			
subjects affected / exposed	0 / 1666 (0.00%)	1 / 1667 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

Brain herniation			
subjects affected / exposed	0 / 1666 (0.00%)	1 / 1667 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Skull fracture			
subjects affected / exposed	0 / 1666 (0.00%)	1 / 1667 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Liver function test abnormal			
subjects affected / exposed	0 / 1666 (0.00%)	1 / 1667 (0.06%)	
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			
Glucose-6-phosphate dehydrogenase deficiency			
subjects affected / exposed	3 / 1666 (0.18%)	1 / 1667 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heart disease congenital			
subjects affected / exposed	0 / 1666 (0.00%)	2 / 1667 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Thalassaemia beta			
subjects affected / exposed	2 / 1666 (0.12%)	0 / 1667 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular septal defect			
subjects affected / exposed	0 / 1666 (0.00%)	2 / 1667 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial septal defect			
subjects affected / exposed	0 / 1666 (0.00%)	1 / 1667 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cortical dysplasia			
subjects affected / exposed	1 / 1666 (0.06%)	0 / 1667 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hydrocele			
subjects affected / exposed	1 / 1666 (0.06%)	0 / 1667 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Patent ductus arteriosus			
subjects affected / exposed	0 / 1666 (0.00%)	1 / 1667 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thalassaemia			
subjects affected / exposed	1 / 1666 (0.06%)	0 / 1667 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Myocarditis			
subjects affected / exposed	1 / 1666 (0.06%)	0 / 1667 (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			
Convulsion			
subjects affected / exposed	1 / 1666 (0.06%)	1 / 1667 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile convulsion			
subjects affected / exposed	0 / 1666 (0.00%)	2 / 1667 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haematoma			
subjects affected / exposed	0 / 1666 (0.00%)	1 / 1667 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

Epilepsy			
subjects affected / exposed	1 / 1666 (0.06%)	0 / 1667 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extrapyramidal disorder			
subjects affected / exposed	0 / 1666 (0.00%)	1 / 1667 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	1 / 1666 (0.06%)	0 / 1667 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hydrocephalus			
subjects affected / exposed	0 / 1666 (0.00%)	1 / 1667 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 1666 (0.00%)	1 / 1667 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ureteric stenosis			
subjects affected / exposed	1 / 1666 (0.06%)	0 / 1667 (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			
Deficiency anaemia			
subjects affected / exposed	0 / 1666 (0.00%)	1 / 1667 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenitis			
subjects affected / exposed	0 / 1666 (0.00%)	1 / 1667 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia			

subjects affected / exposed	2 / 1666 (0.12%)	3 / 1667 (0.18%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Enteritis			
subjects affected / exposed	44 / 1666 (2.64%)	73 / 1667 (4.38%)	
occurrences causally related to treatment / all	0 / 44	0 / 73	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	4 / 1666 (0.24%)	11 / 1667 (0.66%)	
occurrences causally related to treatment / all	0 / 4	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastrointestinal disorder			
subjects affected / exposed	1 / 1666 (0.06%)	3 / 1667 (0.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia, obstructive			
subjects affected / exposed	1 / 1666 (0.06%)	1 / 1667 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	0 / 1666 (0.00%)	2 / 1667 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intussusception			
subjects affected / exposed	1 / 1666 (0.06%)	1 / 1667 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspepsia			
subjects affected / exposed	0 / 1666 (0.00%)	1 / 1667 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Food poisoning			

subjects affected / exposed	0 / 1666 (0.00%)	1 / 1667 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 1666 (0.00%)	1 / 1667 (0.06%)	
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 / 1666 (0.00%)	1 / 1667 (0.06%)	
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	1 / 1666 (0.06%)	0 / 1667 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis diaper			
subjects affected / exposed	1 / 1666 (0.06%)	1 / 1667 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			
subjects affected / exposed	1 / 1666 (0.06%)	0 / 1667 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Hydronephrosis			
subjects affected / exposed	1 / 1666 (0.06%)	0 / 1667 (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			
Bronchitis			

subjects affected / exposed	74 / 1666 (4.44%)	98 / 1667 (5.88%)	
occurrences causally related to treatment / all	0 / 74	0 / 98	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			
subjects affected / exposed	58 / 1666 (3.48%)	61 / 1667 (3.66%)	
occurrences causally related to treatment / all	0 / 58	0 / 61	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumonia			
subjects affected / exposed	14 / 1666 (0.84%)	14 / 1667 (0.84%)	
occurrences causally related to treatment / all	0 / 14	0 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			
subjects affected / exposed	2 / 1666 (0.12%)	8 / 1667 (0.48%)	
occurrences causally related to treatment / all	0 / 2	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand-foot-and-mouth disease			
subjects affected / exposed	5 / 1666 (0.30%)	4 / 1667 (0.24%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheitis			
subjects affected / exposed	4 / 1666 (0.24%)	4 / 1667 (0.24%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute tonsillitis			
subjects affected / exposed	5 / 1666 (0.30%)	2 / 1667 (0.12%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Candidiasis			
subjects affected / exposed	3 / 1666 (0.18%)	1 / 1667 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			

subjects affected / exposed	2 / 1666 (0.12%)	2 / 1667 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngitis			
subjects affected / exposed	2 / 1666 (0.12%)	2 / 1667 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea infectious			
subjects affected / exposed	1 / 1666 (0.06%)	2 / 1667 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus infection			
subjects affected / exposed	2 / 1666 (0.12%)	0 / 1667 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis bacterial			
subjects affected / exposed	0 / 1666 (0.00%)	2 / 1667 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpangina			
subjects affected / exposed	1 / 1666 (0.06%)	1 / 1667 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia klebsiella			
subjects affected / exposed	2 / 1666 (0.12%)	0 / 1667 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicella			
subjects affected / exposed	2 / 1666 (0.12%)	0 / 1667 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial diarrhoea			

subjects affected / exposed	0 / 1666 (0.00%)	1 / 1667 (0.06%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Central nervous system infection				
subjects affected / exposed	1 / 1666 (0.06%)	0 / 1667 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 1	0 / 0		
Infectious mononucleosis				
subjects affected / exposed	1 / 1666 (0.06%)	0 / 1667 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Lobar pneumonia				
subjects affected / exposed	0 / 1666 (0.00%)	1 / 1667 (0.06%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Meningitis				
subjects affected / exposed	1 / 1666 (0.06%)	0 / 1667 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 1		
Otitis media				
subjects affected / exposed	1 / 1666 (0.06%)	0 / 1667 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Pneumonia staphylococcal				
subjects affected / exposed	1 / 1666 (0.06%)	0 / 1667 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
Shigella infection				
subjects affected / exposed	0 / 1666 (0.00%)	1 / 1667 (0.06%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Tracheobronchitis				

subjects affected / exposed	1 / 1666 (0.06%)	0 / 1667 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	16 / 1666 (0.96%)	26 / 1667 (1.56%)	
occurrences causally related to treatment / all	0 / 16	0 / 26	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			
subjects affected / exposed	1 / 1666 (0.06%)	1 / 1667 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hypokalaemia			
subjects affected / exposed	1 / 1666 (0.06%)	3 / 1667 (0.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acidosis			
subjects affected / exposed	0 / 1666 (0.00%)	2 / 1667 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 1666 (0.06%)	0 / 1667 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			
subjects affected / exposed	0 / 1666 (0.00%)	1 / 1667 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	1 / 1666 (0.06%)	3 / 1667 (0.18%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
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	415 / 1666 (24.91%)	448 / 1667 (26.87%)	
General disorders and administration site conditions			
Cough/runny nose			
alternative assessment type: Systematic			
subjects affected / exposed[1]	313 / 1513 (20.69%)	366 / 1514 (24.17%)	
occurrences (all)	313	366	
Diarrhoea			
alternative assessment type: Systematic			
subjects affected / exposed[2]	127 / 1513 (8.39%)	123 / 1514 (8.12%)	
occurrences (all)	127	123	
Irritability/Fussiness			
alternative assessment type: Systematic			
subjects affected / exposed[3]	415 / 1513 (27.43%)	448 / 1514 (29.59%)	
occurrences (all)	415	448	
Loss of appetite			
alternative assessment type: Systematic			
subjects affected / exposed[4]	253 / 1513 (16.72%)	250 / 1514 (16.51%)	
occurrences (all)	253	250	
Fever (GSK scale) (Axillary T >= 37.5°C)			
alternative assessment type: Systematic			
subjects affected / exposed[5]	83 / 1513 (5.49%)	104 / 1514 (6.87%)	
occurrences (all)	83	104	
Vomiting			
alternative assessment type: Systematic			
subjects affected / exposed[6]	213 / 1513 (14.08%)	232 / 1514 (15.32%)	
occurrences (all)	213	232	
Pain			
alternative assessment type: Systematic			

subjects affected / exposed[7]	14 / 150 (9.33%)	9 / 151 (5.96%)	
occurrences (all)	14	9	
Redness			
alternative assessment type: Systematic			
subjects affected / exposed[8]	20 / 150 (13.33%)	13 / 151 (8.61%)	
occurrences (all)	20	13	
Swelling			
alternative assessment type: Systematic			
subjects affected / exposed[9]	13 / 150 (8.67%)	6 / 151 (3.97%)	
occurrences (all)	13	6	
Drowsiness			
alternative assessment type: Systematic			
subjects affected / exposed[10]	44 / 153 (28.76%)	38 / 153 (24.84%)	
occurrences (all)	44	38	
Irritability/Fussiness (OPV and DTPa vaccine)			
alternative assessment type: Systematic			
subjects affected / exposed[11]	56 / 153 (36.60%)	52 / 153 (33.99%)	
occurrences (all)	56	52	
Loss of appetite (OPV and DTPa vaccine)			
alternative assessment type: Systematic			
subjects affected / exposed[12]	43 / 153 (28.10%)	32 / 153 (20.92%)	
occurrences (all)	43	32	
Fever – Chinese scale: Axillary T >= 37.1°C			
alternative assessment type: Systematic			
subjects affected / exposed[13]	302 / 1513 (19.96%)	313 / 1514 (20.67%)	
occurrences (all)	302	313	
Gastrointestinal symptoms			
alternative assessment type: Systematic			
subjects affected / exposed[14]	43 / 153 (28.10%)	38 / 153 (24.84%)	
occurrences (all)	43	38	
Fever – Chinese scale: Axillary T >= 37.1°C (OPV and DTPa vaccine)			
alternative assessment type: Systematic			

subjects affected / exposed[15]	18 / 153 (11.76%)	20 / 153 (13.07%)	
occurrences (all)	18	20	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	119 / 1666 (7.14%)	124 / 1667 (7.44%)	
occurrences (all)	119	124	
Nasopharyngitis			
subjects affected / exposed	103 / 1666 (6.18%)	123 / 1667 (7.38%)	
occurrences (all)	103	123	

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: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively)

[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: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively)

[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: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively)

[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: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively)

[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: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively)

[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: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively)

[7] - 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: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively)

[8] - 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: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively)

[9] - 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: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively)

[10] - 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: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant

medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively)
[11] - 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: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively)
[12] - 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: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively)
[13] - 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: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively)
[14] - 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: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively)
[15] - 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: Subjects who missed reporting symptoms (solicited/unsolicited or concomitant medications) were treated as subjects without symptoms (solicited/unsolicited or concomitant medications, respectively)

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 August 2011	Based on the preliminary review of GE episodes reported to date prior to unblinding and complete cleaning of the database, the rotavirus (RV) attack rate seems lower than what was anticipated in the protocol. In order to have the acceptable statistical power for the primary endpoint, the efficacy follow-up was extended till April 2012 (i.e. end of RV season in China).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported