



## Clinical trial results:

**An open, multicentric, post-marketing surveillance study to evaluate the safety and reactogenicity of GlaxoSmithKline Biologicals' live attenuated oral Human Rotavirus (HRV) vaccine, Rotarix when administered according to the Prescribing Information, in Filipino subjects aged at least 6 weeks at the time of first vaccination.**

### Summary

EudraCT number	2012-004039-21
Trial protocol	Outside EU/EEA
Global end of trial date	17 July 2010

### Results information

Result version number	v1
This version publication date	20 April 2016
First version publication date	15 July 2015

### Trial information

#### Trial identification

Sponsor protocol code	103366
-----------------------	--------

#### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00353366
WHO universal trial number (UTN)	-

Notes:

### Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com

Notes:

### Paediatric regulatory details

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

Notes:

---

**Results analysis stage**

---

Analysis stage	Final
Date of interim/final analysis	07 August 2012
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 March 2010
Global end of trial reached?	Yes
Global end of trial date	17 July 2010
Was the trial ended prematurely?	No

Notes:

---

---

**General information about the trial**

---

Main objective of the trial:

To assess the safety and reactogenicity of GSK Biologicals' Rotavirus vaccine, Rotarix™.

---

Protection of trial subjects:

All 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 vaccine.

---

Background therapy: -

---

Evidence for comparator: -

---

Actual start date of recruitment	16 November 2006
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	Philippines: 1439
Worldwide total number of subjects	1439
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)	1439
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 Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

### Arms

Arm title	Rotarix Group
-----------	---------------

Arm description:

Subjects received 2 doses of Rotarix™ administered at an interval of not less than 4 weeks between the doses. The first dose was administered at the age of 6 weeks and the vaccination course completed by the age of 24 weeks.

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 of the oral vaccine.

Number of subjects in period 1	Rotarix Group
Started	1439
Completed	1296
Not completed	143
Adverse event, serious fatal	5
Consent withdrawn by subject	12
Adverse event, non-fatal	3
Migrated/moved from study area	27
Unspecified	19
Lost to follow-up	65
Protocol deviation	12



## Baseline characteristics

### Reporting groups

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

Reporting group description:

Subjects received 2 doses of Rotarix™ administered at an interval of not less than 4 weeks between the doses. The first dose was administered at the age of 6 weeks and the vaccination course completed by the age of 24 weeks.

Reporting group values	Rotarix Group	Total	
Number of subjects	1439	1439	
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	11.2		
standard deviation	± 3.88	-	
Gender categorical			
Units: Subjects			
Female	692	692	
Male	747	747	

## End points

### End points reporting groups

Reporting group title	Rotarix Group
Reporting group description: Subjects received 2 doses of Rotarix™ administered at an interval of not less than 4 weeks between the doses. The first dose was administered at the age of 6 weeks and the vaccination course completed by the age of 24 weeks.	

### Primary: Number of subjects reporting grade 2 or 3 symptoms (fever, vomiting or diarrhea).

End point title	Number of subjects reporting grade 2 or 3 symptoms (fever, vomiting or diarrhea). <sup>[1]</sup>
End point description: Grade 2 or 3 symptoms assessed include fever, vomiting and diarrhea. Grade 2: an adverse event (AE) which was sufficiently discomforting to interfere with normal everyday activities. Grade 3: an unsolicited AE that prevented normal everyday activity.	
End point type	Primary
End point timeframe: During the 15-day (Days 0-14) solicited follow-up period after each vaccine dose (Dose 1 and Dose 2).	
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			
Subject group type	Reporting group			
Number of subjects analysed	1439			
Units: Subjects				
Grade 2/3; Dose 1 (N=1439)	147			
Grade 2/3; Dose 2 (N=1304)	98			
Grade 2/3; Across Doses (N=1439)	212			

### 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 symptoms assessed included cough, diarrhea, fever, irritability, loss of appetite and vomiting. Any = Any reports of the specified symptom irrespective of intensity grade and relationship to vaccination. Grade 3 symptom: symptom that prevented normal activity. Grade 3 loss of appetite = not eating at all, grade 3 fever = axillary temperature > 39.0°C, grade 3 vomiting = ≥ 3 episodes of vomiting/day and grade 3 diarrhea = ≥ 6 looser than normal stools/day. Related = symptom assessed by the investigator as causally related to the vaccination regardless of intensity grade.	
End point type	Secondary

End point timeframe:

During the 15-day solicited follow-up period (Day 0 to Day 14) after each vaccine dose (Dose 1 and Dose 2).

<b>End point values</b>	Rotarix Group			
Subject group type	Reporting group			
Number of subjects analysed	1439			
Units: Subjects				
Any Cough; Dose 1 (N=1439)	311			
Grade 3 Cough; Dose 1 (N=1439)	13			
Related Cough; Dose 1 (N=1439)	15			
Any Diarrhea; Dose 1 (N=1439)	69			
Grade 3 Diarrhea; Dose 1 (N=1439)	13			
Related Diarrhea; Dose 1 (N=1439)	26			
Any Temperature; Dose 1 (N=1439)	130			
Grade 3 Temperature; Dose 1 (N=1439)	3			
Related Temperature; Dose 1 (N=1439)	26			
Any Irritability; Dose 1 (N=1439)	464			
Grade 3 Irritability; Dose 1 (N=1439)	36			
Related Irritability; Dose 1 (N=1439)	100			
Any Loss of appetite; Dose 1 (N=1439)	269			
Grade 3 Loss of appetite; Dose 1 (N=1439)	4			
Related Loss of appetite; Dose 1 (N=1439)	74			
Any Vomiting; Dose 1 (N=1439)	190			
Grade 3 Vomiting; Dose 1 (N=1439)	44			
Related Vomiting; Dose 1 (N=1439)	38			
Any Cough; Dose 2 (N=1304)	256			
Grade 3 Cough; Dose 2 (N=1304)	7			
Related Cough; Dose 2 (N=1304)	27			
Any Diarrhea; Dose 2 (N=1304)	38			
Grade 3 Diarrhea; Dose 2 (N=1304)	5			
Related Diarrhea; Dose 2 (N=1304)	14			
Any Temperature; Dose 2 (N=1304)	130			
Grade 3 Temperature; Dose 2 (N=1304)	4			
Related Temperature; Dose 2 (N=1304)	24			
Any Irritability; Dose 2 (N=1304)	307			
Grade 3 Irritability; Dose 2 (N=1304)	24			
Related Irritability; Dose 2 (N=1304)	71			
Any Loss of appetite; Dose 2 (N=1304)	193			
Grade 3 Loss of appetite; Dose 2 (N=1304)	5			
Related Loss of appetite; Dose 2 (N=1304)	43			
Any Vomiting; Dose 2 (N=1304)	113			
Grade 3 Vomiting; Dose 2 (N=1304)	13			
Related Vomiting; Dose 2 (N=1304)	22			
Any Cough; Across Doses (N=1439)	443			
Grade 3 Cough; Across Doses (N=1439)	18			

Related Cough; Across Doses (N=1439)	39			
Any Diarrhea; Across Doses (N=1439)	93			
Grade 3 Diarrhea; Across Doses (N=1439)	18			
Related Diarrhea; Across Doses (N=1439)	36			
Any Temperature; Across Doses (N=1439)	226			
Grade 3 Temperature; Across Doses (N=1439)	7			
Related Temperature; Across Doses (N=1439)	48			
Any Irritability; Across Doses (N=1439)	545			
Grade 3 Irritability; Across Doses (N=1439)	51			
Related Irritability; Across Doses (N=1439)	130			
Any Loss of appetite; Across Doses (N=1439)	351			
Grade 3 Loss of appetite; Across Doses (N=1439)	8			
Related Loss of appetite; Across Doses (N=1439)	93			
Any Vomiting; Across Doses (N=1439)	240			
Grade 3 Vomiting; Across Doses (N=1439)	54			
Related Vomiting; Across Doses (N=1439)	49			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Number of subjects reporting any unsolicited Adverse Event (AE)

End point title	Number of subjects reporting any unsolicited Adverse Event (AE)
-----------------	---

End point description:

An unsolicited AE covers any untoward medical occurrence in a clinical investigation subject temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product. Any was defined as an adverse event (AE) reported in addition to those solicited during the clinical study. Any solicited symptom with onset outside the specified period of follow-up for solicited symptoms was reported as an unsolicited adverse event.

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

End point timeframe:

During the 31-day follow-up period (Day 0 to Day 30) after any vaccine dose.



<b>End point values</b>	Rotarix Group			
Subject group type	Reporting group			
Number of subjects analysed	1439			
Units: Subjects				
any AE (s)	352			

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects reporting serious adverse events (SAE)

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

End point description:

Serious adverse events (SAEs) assessed include medical occurrences that resulted in death, were life threatening, required hospitalization or prolongation of hospitalization, resulted in disability/incapacity or was a congenital anomaly/birth defect in the offspring of a study subject.

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

End point timeframe:

Throughout the study period (Day 0 to one month post-Dose 2).

<b>End point values</b>	Rotarix Group			
Subject group type	Reporting group			
Number of subjects analysed	1439			
Units: Subjects				
any SAE (s)	32			

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Serious Adverse Events: during the entire study period; Solicited local and general symptoms: During the 15-day (Days 0-14) post-vaccination period; Unsolicited symptoms: During the 31-day (Days 0-30) post-vaccination period.

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	15.0
--------------------	------

### Reporting groups

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

Reporting group description:

Subjects received 2 doses of Rotarix<sup>TM</sup> administered at an interval of not less than 4 weeks between the doses. The first dose was administered at the age of 6 weeks and the vaccination course completed by the age of 24 weeks.

Serious adverse events	Rotarix Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	32 / 1439 (2.22%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Nervous system disorders			
Hypersomnia			
subjects affected / exposed	1 / 1439 (0.07%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypophagia			
subjects affected / exposed	1 / 1439 (0.07%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Milk Allergy			
subjects affected / exposed	1 / 1439 (0.07%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 1439 (0.07%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intussusception			
subjects affected / exposed	1 / 1439 (0.07%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 1439 (0.07%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia aspiration			
subjects affected / exposed	1 / 1439 (0.07%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Exanthema subitum			
subjects affected / exposed	1 / 1439 (0.07%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchopneumonia			
subjects affected / exposed	8 / 1439 (0.56%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 0		
Urinary Tract Infection			
subjects affected / exposed	5 / 1439 (0.35%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Amoebic Dysentery			

subjects affected / exposed	4 / 1439 (0.28%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	4 / 1439 (0.28%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Amoebiasis			
subjects affected / exposed	2 / 1439 (0.14%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Bronchiolitis			
subjects affected / exposed	1 / 1439 (0.07%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	1 / 1439 (0.07%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diarrhoea Infections			
subjects affected / exposed	1 / 1439 (0.07%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	1 / 1439 (0.07%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia bacterial			
subjects affected / exposed	1 / 1439 (0.07%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Roseola			

subjects affected / exposed	1 / 1439 (0.07%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection enterococcal			
subjects affected / exposed	1 / 1439 (0.07%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Viral rash			
subjects affected / exposed	1 / 1439 (0.07%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

<b>Non-serious adverse events</b>	Rotarix Group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	545 / 1439 (37.87%)		
General disorders and administration site conditions			
Diarrhea; Across Doses			
alternative assessment type: Systematic			
subjects affected / exposed	93 / 1439 (6.46%)		
occurrences (all)	93		
Cough; Across Doses			
alternative assessment type: Systematic			
subjects affected / exposed	443 / 1439 (30.79%)		
occurrences (all)	443		
Fever; Across Doses			
alternative assessment type: Systematic			
subjects affected / exposed	226 / 1439 (15.71%)		
occurrences (all)	226		
Irritability; Across Doses			
alternative assessment type: Systematic			

subjects affected / exposed	545 / 1439 (37.87%)			
occurrences (all)	545			
Loss of appetite; Across Doses alternative assessment type: Systematic				
subjects affected / exposed	351 / 1439 (24.39%)			
occurrences (all)	351			
Vomiting; Across Doses alternative assessment type: Systematic				
subjects affected / exposed	240 / 1439 (16.68%)			
occurrences (all)	240			
Cough; Dose 1 alternative assessment type: Systematic				
subjects affected / exposed	311 / 1439 (21.61%)			
occurrences (all)	311			
Fever; Dose 1 alternative assessment type: Systematic				
subjects affected / exposed	130 / 1439 (9.03%)			
occurrences (all)	130			
Irritability; Dose 1 alternative assessment type: Systematic				
subjects affected / exposed	464 / 1439 (32.24%)			
occurrences (all)	464			
Loss of appetite; Dose 1 alternative assessment type: Systematic				
subjects affected / exposed	269 / 1439 (18.69%)			
occurrences (all)	269			
Vomiting; Dose 1 alternative assessment type: Systematic				
subjects affected / exposed	190 / 1439 (13.20%)			
occurrences (all)	190			
Cough; Dose 2 alternative assessment type: Systematic				

subjects affected / exposed <sup>[1]</sup>	256 / 1304 (19.63%)		
occurrences (all)	256		
Fever; Dose 2 alternative assessment type: Systematic			
subjects affected / exposed <sup>[2]</sup>	130 / 1304 (9.97%)		
occurrences (all)	130		
Irritability; Dose 2 alternative assessment type: Systematic			
subjects affected / exposed <sup>[3]</sup>	307 / 1304 (23.54%)		
occurrences (all)	307		
Loss of appetite; Dose 2 alternative assessment type: Systematic			
subjects affected / exposed <sup>[4]</sup>	193 / 1304 (14.80%)		
occurrences (all)	193		
Vomiting; Dose 2 alternative assessment type: Systematic			
subjects affected / exposed <sup>[5]</sup>	113 / 1304 (8.67%)		
occurrences (all)	113		

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).

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 April 2008	The age of the infants was changed from between 6 - 14 weeks to at least 6 weeks at the time of the first vaccination. This change was made to reflect the modifications made in the prescribing information. Other changes were made to reflect changes in the contributing authors and contact for reporting serious adverse events. In addition, the sponsor information sheet was removed from the main protocol to avoid further amendments in case of any changes in the future.

Notes:

---

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported