Clinical trial results:
A phase II, randomized, double-blind, placebo-controlled study to evaluate the immunogenicity, reactogenicity and safety of two doses of GlaxoSmithKline (GSK) Biologicals' oral live attenuated human rotavirus (HRV) liquid vaccine, when given to healthy infants, in Philippines

Summary

EudraCT number	2015-001544-11
Trial protocol	Outside EU/EEA
Global end of trial date	04 September 2007

Results information

Result version number	v3 (current)
This version publication date	28 March 2023
First version publication date	08 July 2015
Version creation reason	• Correction of full data set Correction and alignment of full data set.

Trial information

Trial identification

Sponsor protocol code	109216

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00432380
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	04 September 2007
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 September 2007
Global end of trial reached?	Yes
Global end of trial date	04 September 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the immunogenicity of GSK Biologicals' HRV liquid vaccine versus placebo, in terms of anti-rotavirus Immunoglobulin A (IgA) antibody seroconversion at Month 3 (i.e. Visit 4), when administered concomitantly with the second and third routine EPI immunization.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	09 March 2007
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Philippines: 375
Worldwide total number of subjects	375
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)	375
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	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Carer, Subject, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo-Rotarix-Rotarix Group

Arm description:

Healthy male or female infants between, and including, 5 to 10 weeks of age, were administered 2 oral doses of Rotarix liquid vaccine at Month 1 and Month 2, and a single oral dose of placebo at Day 0. Subjects also received routine infant vaccinations according to the Expanded Program of Immunization (EPI) recommendations in Philippines.

Arm type	Experimental
Investigational medicinal product name	Rotarix
Investigational medicinal product code	SUB22357
Other name	HUMAN ROTAVIRUS RIX4414 STRAIN (LIVE ATTENUATED)
Pharmaceutical forms	Powder and solvent for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Two oral doses of the liquid HRV vaccine administered at Months 1 and 2.

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

Dosage and administration details:

1 oral dose of placebo administered at Day 0.

Arm title	Rotarix-Placebo-Rotarix Group

Arm description:

Healthy male or female infants between, and including, 5 to 10 weeks of age, were administered 2 oral doses of Rotarix liquid vaccine at Day 0 and Month 2, and a single oral dose of placebo at Month 1. Subjects also received routine infant vaccinations according to the Expanded Program of Immunization (EPI) recommendations in Philippines.

Arm type	Experimental
Investigational medicinal product name	Rotarix
Investigational medicinal product code	SUB22357
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Pharmaceutical forms	Powder and solvent for oral suspension
Routes of administration	Oral use

Dosage and administration details:	
Two oral doses of the liquid HRV vaccine administered at Day 0 and Month 2.	
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Oral use
Dosage and administration details:	
1 oral dose of placebo administered at Month 1.	
Arm title	Placebo Group
Arm description:	
Healthy male or female infants between, and including, 5 to 10 weeks of age, were administered 3 oral doses of placebo at Day 0, Month 1 and Month 2. Subjects also received routine infant vaccinations according to the Expanded Program of Immunization (EPI) recommendations in Philippines.	
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:	
Three oral doses of placebo administered at Day 0, Months 1 and 2.	

Number of subjects in period 1	Placebo-Rotarix-Rotarix Group	Rotarix-Placebo-Rotarix Group	Placebo Group
Started	150	150	75
Completed	146	146	74
Not completed	4	4	1
Adverse event, non-fatal	1	-	-
Migrated/moved from study area	3	4	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo-Rotarix-Rotarix Group
Reporting group description:	
Healthy male or female infants between, and including, 5 to 10 weeks of age, were administered 2 oral doses of Rotarix liquid vaccine at Month 1 and Month 2, and a single oral dose of placebo at Day 0. Subjects also received routine infant vaccinations according to the Expanded Program of Immunization (EPI) recommendations in Philippines.	
Reporting group title	Rotarix-Placebo-Rotarix Group
Reporting group description:	
Healthy male or female infants between, and including, 5 to 10 weeks of age, were administered 2 oral doses of Rotarix liquid vaccine at Day 0 and Month 2, and a single oral dose of placebo at Month 1. Subjects also received routine infant vaccinations according to the Expanded Program of Immunization (EPI) recommendations in Philippines.	
Reporting group title	Placebo Group
Reporting group description:	
Healthy male or female infants between, and including, 5 to 10 weeks of age, were administered 3 oral doses of placebo at Day 0, Month 1 and Month 2. Subjects also received routine infant vaccinations according to the Expanded Program of Immunization (EPI) recommendations in Philippines.	

Reporting group values	Placebo-Rotarix-Rotarix Group	Rotarix-Placebo-Rotarix Group	Placebo Group
Number of subjects	150	150	75
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	150	150	75
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: weeks			
arithmetic mean	6.6	6.5	6.6
standard deviation	± 1.07	± 1	± 1.02
Gender categorical Units: Subjects			
Female	59	76	40
Male	91	74	35

Reporting group values	Total		
Number of subjects	375		
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)	375		
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			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	175		
Male	200		

End points

End points reporting groups

Reporting group title	Placebo-Rotarix-Rotarix Group
Reporting group description:	
Healthy male or female infants between, and including, 5 to 10 weeks of age, were administered 2 oral doses of Rotarix liquid vaccine at Month 1 and Month 2, and a single oral dose of placebo at Day 0. Subjects also received routine infant vaccinations according to the Expanded Program of Immunization (EPI) recommendations in Philippines.	
Reporting group title	Rotarix-Placebo-Rotarix Group
Reporting group description:	
Healthy male or female infants between, and including, 5 to 10 weeks of age, were administered 2 oral doses of Rotarix liquid vaccine at Day 0 and Month 2, and a single oral dose of placebo at Month 1. Subjects also received routine infant vaccinations according to the Expanded Program of Immunization (EPI) recommendations in Philippines.	
Reporting group title	Placebo Group
Reporting group description:	
Healthy male or female infants between, and including, 5 to 10 weeks of age, were administered 3 oral doses of placebo at Day 0, Month 1 and Month 2. Subjects also received routine infant vaccinations according to the Expanded Program of Immunization (EPI) recommendations in Philippines.	

Primary: Number of seroconverted subjects for Anti-rotavirus (Anti-RV) Immunoglobulin A (IgA) Antibody

End point title	Number of seroconverted subjects for Anti-rotavirus (Anti-RV) Immunoglobulin A (IgA) Antibody[1][2]
End point description:	
Seroconversion was defined as the appearance of anti-RV IgA antibody concentrations greater than or equal to (≥) 20 units per milliliter (U/mL) in subjects initially (i.e. prior to the first dose of Rotarix vaccine or placebo) seronegative, when administered concomitantly with the second and third routine EPI immunization. This outcome measure only concerns subjects in the Placebo-Rotarix-Rotarix Group.	
End point type	Primary
End point timeframe:	
At Month 3	

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: No statistical analyses for this end point.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analyses for this end point.

End point values	Placebo-Rotarix-Rotarix Group			
Subject group type	Reporting group			
Number of subjects analysed	120			
Units: Subjects				
Anti-RV IgA	84			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted subjects for Anti-RV IgA antibody

End point title	Number of seroconverted subjects for Anti-RV IgA antibody[3]

End point description:

Seroconversion was defined as the appearance of anti-RV IgA antibody concentrations ≥ 20 U/mL in subjects initially (i.e. prior to the first dose of Rotarix vaccine or placebo) seronegative, when administered concomitantly with the first and third routine EPI immunization. This outcome measure only concerns subjects in the Rotarix-Placebo-Rotarix Group.

End point type	Secondary

End point timeframe:

At Month 3

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analyses for this end point.

End point values	Rotarix-Placebo-Rotarix Group			
Subject group type	Reporting group			
Number of subjects analysed	120			
Units: Subjects				
Anti-RV IgA	71			

Statistical analyses

No statistical analyses for this end point

Secondary: Serum IgA Antibody Concentrations Against Rotavirus

End point title	Serum IgA Antibody Concentrations Against Rotavirus[4]

End point description:

Antibody concentrations were presented as geometric mean concentrations (GMCs), expressed in units per milliliter (U/mL). This outcome measure only concerns subjects in Placebo-Rotarix-Rotarix and Rotarix-Placebo-Rotarix Groups.

End point type	Secondary

End point timeframe:

At Month 3

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No statistical analyses for this end point.

End point values	Placebo-Rotarix-Rotarix Group	Rotarix-Placebo-Rotarix Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	120	120		
Units: U/mL				
geometric mean (confidence interval 95%)				
Anti-rotavirus IgA antibody GMC	68 (50.1 to 92.1)	75.6 (52.5 to 109)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting grade "2" or grade "3" fever, vomiting or diarrhea

End point title	Number of subjects reporting grade "2" or grade "3" fever, vomiting or diarrhea

End point description:

Any symptom = occurrence of the symptom (i.e. fever or vomiting or diarrhea) regardless of intensity grade or relationship to vaccination. Grade 2 fever = Rectal temperature greater than (>) 38.5 – less than or equal to (≤) 39.5 degrees Celsius (°C) or axillary temperature > 38.0 – ≤ 39.0°C, Grade 3 fever = Rectal temperature > 39.5°C or axillary temperature > 39.0°C. Grade 2 vomiting = 2 episodes of vomiting/ day. Grade 3 vomiting = 3 or more episodes of vomiting/ day. Grade 2 diarrhea = 4-5 looser than normal stools/ day. Grade 3 diarrhea = 6 or more looser than normal stools/ day.

End point type	Secondary

End point timeframe:

During the 8-day (Day 0-Day 7) period following each dose of study vaccine or placebo and across doses

End point values	Placebo-Rotarix-Rotarix Group	Rotarix-Placebo-Rotarix Group	Placebo Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	150	150	75	
Units: Subjects				
Any symptom, Dose 1 [N=150, 150, 75]	57	68	35	
Any symptom, Dose 2 [N=149, 147, 75]	52	36	19	
Any symptom, Dose 3 [N= 146, 147, 75]	29	38	24	
Any symptom, Across doses [N= 150, 150, 75]	86	91	48	

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:

Assessed solicited general symptoms were cough/runny nose, diarrhea, fever (rectally), irritability, loss of appetite and vomiting. Any = occurrence of the symptom regardless of intensity grade or relationship to vaccination. Grade 3 Cough/runny nose = cough/runny nose which prevented daily activity, Grade 2 Diarrhea: 4-5 looser than normal stools/ day, Grade 3 Diarrhea = ≥ 6 looser than normal stools/ day, Grade 3 Irritability = crying that could not be comforted/ prevented normal activity, Grade 3 Loss of appetite = not eating at all, Grade 2 Vomiting= 2 episodes of vomiting/ day and Grade 3 Vomiting = ≥ 3 episodes of vomiting/ day. Related = symptom considered by the investigator to have a causal relationship to study vaccination.

End point type	Secondary

End point timeframe:

During the 8-day (Day 0-Day 7) period following each dose of study vaccine or placebo and across doses

End point values	Placebo-Rotarix-Rotarix Group	Rotarix-Placebo-Rotarix Group	Placebo Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	150	150	75	
Units: Subjects				
Between Dose 1 and before Dose 2 [N=150, 150, 75]	1	0	1	
Between Dose 2 and before Dose 3 [N=149, 147, 75]	0	0	0	
Between Dose 3 and Month 3 [N=146, 147, 75]	0	0	0	
Between Dose 1 and Month 3 [N=150, 150, 75]	1	0	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited adverse event

End point title	Number of subjects reporting any unsolicited adverse event

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 (Day 0-Day 30) period following any study vaccine dose or placebo

End point values	Placebo-Rotarix-Rotarix Group	Rotarix-Placebo-Rotarix Group	Placebo Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	150	150	75	
Units: Subjects				
Any AE(s)	53	60	19	

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Serious adverse events (SAEs) assessed include any untoward medical occurrences that results in death, are life threatening, requires hospitalization or prolongation of hospitalization, result in disability/incapacity or congenital anomaly/birth defect in the offspring of a study subject.

End point type	Secondary

End point timeframe:

During the entire study period (from Day 0 to Month 3)

End point values	Placebo-Rotarix-Rotarix Group	Rotarix-Placebo-Rotarix Group	Placebo Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	150	150	75	
Units: Subjects				
Any SAE(s)	1	1	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 3).

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	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10.1

Reporting groups

Reporting group title	Placebo-Rotarix-Rotarix Group

Reporting group description:

Healthy male or female infants between, and including, 5 to 10 weeks of age, were administered 2 oral doses of Rotarix liquid vaccine at Month 1 and Month 2, and a single oral dose of placebo at Day 0. Subjects also received routine infant vaccinations according to the Expanded Program of Immunization (EPI) recommendations in Philippines.

Reporting group title	Rotarix-Placebo-Rotarix Group

Reporting group description:

Healthy male or female infants between, and including, 5 to 10 weeks of age, were administered 2 oral doses of Rotarix liquid vaccine at Day 0 and Month 2, and a single oral dose of placebo at Month 1. Subjects also received routine infant vaccinations according to the Expanded Program of Immunization (EPI) recommendations in Philippines.

Reporting group title	Placebo Group

Reporting group description:

Healthy male or female infants between, and including, 5 to 10 weeks of age, were administered 3 oral doses of placebo at Day 0, Month 1 and Month 2. Subjects also received routine infant vaccinations according to the Expanded Program of Immunization (EPI) recommendations in Philippines.

Serious adverse events	Placebo-Rotarix-Rotarix Group	Rotarix-Placebo-Rotarix Group	Placebo Group
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 150 (0.67%)	1 / 150 (0.67%)	1 / 75 (1.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Immune system disorders			
Milk allergy			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 150 (0.00%)	1 / 150 (0.67%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			

Gastroenteritis salmonella			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 150 (0.67%)	0 / 150 (0.00%)	0 / 75 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 150 (0.00%)	0 / 150 (0.00%)	1 / 75 (1.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Placebo-Rotarix-Rotarix Group	Rotarix-Placebo-Rotarix Group	Placebo Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	139 / 150 (92.67%)	137 / 150 (91.33%)	69 / 75 (92.00%)
General disorders and administration site conditions			
Cough/runny nose			
subjects affected / exposed	82 / 150 (54.67%)	69 / 150 (46.00%)	40 / 75 (53.33%)
occurrences (all)	82	69	40
Diarrhea			
subjects affected / exposed	8 / 150 (5.33%)	6 / 150 (4.00%)	7 / 75 (9.33%)
occurrences (all)	8	6	7
Fever (Rectally)			
subjects affected / exposed	139 / 150 (92.67%)	137 / 150 (91.33%)	69 / 75 (92.00%)
occurrences (all)	139	137	69
Irritability			
subjects affected / exposed	93 / 150 (62.00%)	78 / 150 (52.00%)	40 / 75 (53.33%)
occurrences (all)	93	78	40
Loss of appetite			
subjects affected / exposed	40 / 150 (26.67%)	46 / 150 (30.67%)	23 / 75 (30.67%)
occurrences (all)	40	46	23
Vomiting			

subjects affected / exposed	35 / 150 (23.33%)	32 / 150 (21.33%)	9 / 75 (12.00%)
occurrences (all)	35	32	9
Infections and infestations			
Upper respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	19 / 150 (12.67%)	21 / 150 (14.00%)	6 / 75 (8.00%)
occurrences (all)	19	21	6
Rhinitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	13 / 150 (8.67%)	16 / 150 (10.67%)	6 / 75 (8.00%)
occurrences (all)	13	16	6
Bronchitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	7 / 150 (4.67%)	7 / 150 (4.67%)	4 / 75 (5.33%)
occurrences (all)	7	7	4
Diarrhea infectious			
alternative assessment type: Non-systematic			
subjects affected / exposed	5 / 150 (3.33%)	9 / 150 (6.00%)	2 / 75 (2.67%)
occurrences (all)	5	9	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 January 2007	It was decided to offer all subjects complementary vaccination against Haemophilus influenzae type b (Hib) disease with GSK Biologicals' Hiberix vaccine after the study end. The protocol was amended to reflect this change.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported