Clinical trial results:
Open, multi-centric, post-marketing surveillance (PMS) to evaluate the reactogenicity and safety of two doses of GlaxoSmithKline (GSK) Biologicals' oral live attenuated human rotavirus (HRV) vaccine, Rotarix™ when administered according to a 0, 2 month schedule to Sri Lankan infants aged at least 6 weeks at the time of first vaccination.

Summary

EudraCT number	2015-001546-28
Trial protocol	Outside EU/EEA
Global end of trial date	26 August 2009

Results information

Result version number	v1
This version publication date	20 April 2016
First version publication date	10 July 2015

Trial information

Trial identification

Sponsor protocol code	111664

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00779779
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	13 January 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 May 2009
Global end of trial reached?	Yes
Global end of trial date	26 August 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the reactogenicity of Rotarix™ in terms of occurrence of at least one grade "2" or grade "3" fever, vomiting or diarrhoea within a 8-day follow-up period after each vaccine dose.

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	22 November 2008
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	Sri Lanka: 522
Worldwide total number of subjects	522
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)	522
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

During the screening the following steps occurred: check for inclusion/exclusion criteria, contraindications/precautions, medical history of the subjects and signing informed consent forms.

Period 1

Period 1 title	Overall period (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Rotarix Group

Arm description:

Subjects received 2 oral doses of Rotarix vaccine at an interval of at least 4 weeks between doses. The first dose was given from the age of 6 weeks and vaccination with both doses was to be completed by 24 weeks of age.

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

Dosage and administration details:

Two oral doses, with at least 4 weeks interval in-between.

Number of subjects in period 1	Rotarix Group
Started	522
Completed	498
Not completed	24
Consent withdrawn by subject	4
Adverse event, non-fatal	1
Protocol Violation	14
Lost to follow-up	5

Baseline characteristics

Reporting groups	
Reporting group title	Rotarix Group
Reporting group description:	
Subjects received 2 oral doses of Rotarix vaccine at an interval of at least 4 weeks between doses. The first dose was given from the age of 6 weeks and vaccination with both doses was to be completed by 24 weeks of age.	

Reporting group values	Rotarix Group	Total	
Number of subjects	522	522	
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	12.5		
standard deviation	± 5.62	-	
Gender categorical Units: Subjects			
Female	267	267	
Male	255	255	

End points

End points reporting groups

Reporting group title	Rotarix Group

Reporting group description:

Subjects received 2 oral doses of Rotarix vaccine at an interval of at least 4 weeks between doses. The first dose was given from the age of 6 weeks and vaccination with both doses was to be completed by 24 weeks of age.

Primary: Number of subjects reporting Grade 2 or 3 symptoms (fever, vomiting, diarrhoea)

End point title	Number of subjects reporting Grade 2 or 3 symptoms (fever, vomiting, diarrhoea)[1]

End point description:

Grade 2 fever was defined as axillary temperature > 38.0 to <= 39.0 degrees Celsius and grade 3 fever as axillary temperature > 39.0 degrees Celsius. Grade 2 vomiting was defined as 2 episodes of vomiting per day and grade 3 as 3 or more episodes of vomiting per day. Grade 2 diarrhoea was defined as 4-5 looser than normal stools per day and grade 3 as 6 or more looser than normal stools a day.

End point type	Primary

End point timeframe:

During the 8-day 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	522			
Units: Subjects				
Grade 2/3 fever, vomiting or diarrhoea; Dose 1	46			
Grade 2/3 fever, vomiting or diarrhoea; Dose 2	50			
Grade 2/3 fever,vomiting or diarrhoea;Across doses	78			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any, related and grade 3 solicited general symptoms

End point title	Number of subjects reporting any, related and grade 3 solicited general symptoms

End point description:

Assessed solicited general symptoms were cough, diarrhoea, irritability, loss of appetite, fever (degrees Celsius) and vomiting. Any = occurrence of the symptom regardless of intensity and relationship to vaccination. Grade 3 Cough and Irritability = symptoms which prevented normal everyday activities. Grade 3 Diarrhoea = ≥ 6 looser than normal stools/day. 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. Related = considered by the investigator to be causally related to the study vaccination.

End point type	Secondary

End point timeframe:

During the 8-day follow-up period after each vaccine dose (Dose 1 and Dose 2).

End point values	Rotarix Group			
Subject group type	Reporting group			
Number of subjects analysed	522			
Units: Subjects				
Any Cough; Dose 1 [N=522]	43			
Grade 3 Cough; Dose 1 [N=522]	2			
Related Cough; Dose 1 [N=522]	43			
Any Diarrhoea; Dose 1 [N=522]	18			
Grade 3 Diarrhoea; Dose 1 [N=522]	7			
Related Diarrhoea; Dose 1 [N=522]	17			
Any Irritability; Dose 1 [N=522]	81			
Grade 3 Irritability; Dose 1 [N=522]	4			
Related Irritability; Dose 1 [N=522]	81			
Any Loss of appetite; Dose 1 [N=522]	54			
Grade 3 Loss of appetite; Dose 1 [N=522]	0			
Related Loss of appetite; Dose 1 [N=522]	54			
Any Temperature; Dose 1 [N=522]	94			
Grade 3 Temperature; Dose 1 [N=522]	3			
Related Temperature; Dose 1 [N=522]	94			
Any Vomiting; Dose 1 [N=522]	28			
Grade 3 Vomiting; Dose 1 [N=522]	9			
Related Vomiting; Dose 1 [N=522]	28			
Any Cough; Dose 2 [N=501]	42			
Grade 3 Cough; Dose 2 [N=501]	4			
Related Cough; Dose 2 [N=501]	42			
Any Diarrhoea; Dose 2 [N=501]	9			
Grade 3 Diarrhoea; Dose 2 [N=501]	3			
Related Diarrhoea; Dose 2 [N=501]	9			
Any Irritability; Dose 2 [N=501]	84			
Grade 3 Irritability; Dose 2 [N=501]	2			
Related Irritability; Dose 2 [N=501]	83			
Any Loss of appetite; Dose 2 [N=501]	51			
Grade 3 Loss of appetite; Dose 2 [N=501]	1			
Related Loss of appetite; Dose 2 [N=501]	51			
Any Temperature; Dose 2 [N=501]	101			
Grade 3 Temperature; Dose 2 [N=501]	3			
Related Temperature; Dose 2 [N=501]	101			
Any Vomiting; Dose 2 [N=501]	27			
Grade 3 Vomiting; Dose 2 [N=501]	5			
Related Vomiting; Dose 2 [N=501]	27			

Any Cough; Across Doses [N=522]	71			
Grade 3 Cough; Across Doses [N=522]	6			
Related Cough; Across Doses [N=522]	71			
Any Diarrhoea; Across Doses [N=522]	24			
Grade 3 Diarrhoea; Across Doses [N=522]	9			
Related Diarrhoea; Across Doses [N=522]	23			
Any Irritability; Across Doses [N=522]	124			
Grade 3 Irritability; Across Doses [N=522]	6			
Related Irritability; Across Doses [N=522]	123			
Any Loss of appetite; Across Doses [N=522]	83			
Grade 3 Loss of appetite; Across Doses [N=522]	1			
Related Loss of appetite; Across Doses [N=522]	83			
Any Temperature; Across Doses [N=522]	152			
Grade Temperature; Across Doses [N=522]	6			
Related Temperature; Across Doses [N=522]	152			
Any Vomiting; Across Doses [N=522]	45			
Grade 3 Vomiting; Across Doses [N=522]	11			
Related Vomiting; Across Doses [N=522]	45			

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

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 after each vaccine dose.

End point values	Rotarix Group			
Subject group type	Reporting group			
Number of subjects analysed	522			
Units: Subjects				
any AE(s)	25			

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

SAEs assessed include medical occurrences that result in death, is life threatening, require hospitalization or prolongation of hospitalization, result in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subject

End point type	Secondary

End point timeframe:

Throughout the study period (Day 0 to Month 3 or 4)

End point values	Rotarix Group			
Subject group type	Reporting group			
Number of subjects analysed	522			
Units: Subjects				
any SAE(s)	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited general symptoms: during the 8-day (Day 0 - Day7) post-vaccination period. Unsolicited AEs: during the 31-day (Day 0 - Day 30) post-vaccination period and SAEs during the entire period (Day 0 to Month 3 or 4).

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.1

Reporting groups

Reporting group title	Rotarix Group

Reporting group description:

Subjects received 2 oral doses of Rotarix vaccine at an interval of at least 4 weeks between doses. The first dose was given from the age of 6 weeks and vaccination with both doses was to be completed by 24 weeks of age.

Serious adverse events	Rotarix Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 522 (0.19%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Nervous system disorders			
Crying			
subjects affected / exposed	1 / 522 (0.19%)		
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 %

Non-serious adverse events	Rotarix Group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	152 / 522 (29.12%)		
General disorders and administration site conditions			
Cough; Dose 1			
alternative assessment type: Systematic			
subjects affected / exposed	43 / 522 (8.24%)		
occurrences (all)	43		
Loss of appetite; Dose 1			

alternative assessment type: Systematic				
subjects affected / exposed	54 / 522 (10.34%)			
occurrences (all)	54			
Irritability; Dose 1				
alternative assessment type: Systematic				
subjects affected / exposed	81 / 522 (15.52%)			
occurrences (all)	81			
Fever; Dose 1				
alternative assessment type: Systematic				
subjects affected / exposed	94 / 522 (18.01%)			
occurrences (all)	94			
Vomiting; Dose 1				
alternative assessment type: Systematic				
subjects affected / exposed	28 / 522 (5.36%)			
occurrences (all)	28			
Loss of appetite; Dose 2				
alternative assessment type: Systematic				
subjects affected / exposed[1]	51 / 501 (10.18%)			
occurrences (all)	51			
Loss of appetite; Across Doses				
alternative assessment type: Systematic				
subjects affected / exposed	83 / 522 (15.90%)			
occurrences (all)	83			
Irritability; Dose 2				
alternative assessment type: Systematic				
subjects affected / exposed[2]	84 / 501 (16.77%)			
occurrences (all)	84			
Irritability; Across Doses				
alternative assessment type: Systematic				
subjects affected / exposed	124 / 522 (23.75%)			
occurrences (all)	124			
Fever; Dose 2				
alternative assessment type: Systematic				

subjects affected / exposed[3]	101 / 501 (20.16%)		
occurrences (all)	101		
Fever; Across Doses			
alternative assessment type: Systematic			
subjects affected / exposed	152 / 522 (29.12%)		
occurrences (all)	152		
Vomiting; Dose 2			
alternative assessment type: Systematic			
subjects affected / exposed[4]	27 / 501 (5.39%)		
occurrences (all)	27		
Vomiting; Across Doses			
alternative assessment type: Systematic			
subjects affected / exposed	45 / 522 (8.62%)		
occurrences (all)	45		

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: 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)

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported