Clinical trial results:
A phase I, double-blind, randomised, placebo-controlled study to assess the reactogenicity and safety of two doses of GlaxoSmithKline Biologicals' (GSK) oral live attenuated liquid human rotavirus (HRV) vaccine, when administered to healthy infants aged 6 to 16 weeks at the time of the first dose of vaccination according to a 0, 1 month schedule in China.

Summary

EudraCT number	2012-001481-16
Trial protocol	Outside EU/EEA
Global end of trial date	28 June 2010

Results information

Result version number	v1 (current)
This version publication date	18 April 2016
First version publication date	25 June 2015

Trial information

Trial identification

Sponsor protocol code	113518

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01107587
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 44 2089904466, GSKClinicalSupportHD@gsk.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	28 June 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 June 2010
Global end of trial reached?	Yes
Global end of trial date	28 June 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the reactogenicity of GSK Biologicals' liquid HRV vaccine when compared to placebo in terms of grade "3" solicited AEs.

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 the vaccine.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	13 April 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: 50
Worldwide total number of subjects	50
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)	50
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 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	HRV Group

Arm description:

Subjects received 2 oral doses of GlaxoSmithKline (GSK) Biologicals' oral live attenuated liquid human rotavirus (HRV)HRV vaccine according to a 0, 1 month schedule

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

Dosage and administration details:

Two oral doses of the liquid HRV vaccine administered at Months 0 and 1

Arm title	Placebo Group

Arm description:

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

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

Dosage and administration details:

Two oral doses of placebo administered at Months 0 and 1

Number of subjects in period 1	HRV Group	Placebo Group
Started	25	25
Completed	23	22
Not completed	2	3
Consent withdrawn by subject	1	1
Migrated/moved from study area	1	2

Baseline characteristics

Reporting groups	
Reporting group title	HRV Group
Reporting group description:	
Subjects received 2 oral doses of GlaxoSmithKline (GSK) Biologicals' oral live attenuated liquid human rotavirus (HRV)HRV vaccine according to a 0, 1 month schedule	
Reporting group title	Placebo Group
Reporting group description:	
Subjects received 2 oral doses of placebo according to a 0, 1 month schedule.	

Reporting group values	HRV Group	Placebo Group	Total
Number of subjects	25	25	50
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	10.3	11.8	
standard deviation	± 2.7	± 2.43	-
Gender categorical			
Units: Subjects			
Female	13	10	23
Male	12	15	27

End points

End points reporting groups

Reporting group title	HRV Group
Reporting group description:	
Subjects received 2 oral doses of GlaxoSmithKline (GSK) Biologicals' oral live attenuated liquid human rotavirus (HRV)HRV vaccine according to a 0, 1 month schedule	
Reporting group title	Placebo Group
Reporting group description:	
Subjects received 2 oral doses of placebo according to a 0, 1 month schedule.	

Primary: Number of subjects reporting grade 3 solicited general symptoms

End point title	Number of subjects reporting grade 3 solicited general symptoms[1]
End point description:	
Assessed solicited general symptoms were cough, diarrhoea, irritability, loss of appetite, fever (By GSK scale and Chinese scale) and vomiting. Grade 3 cough = Cough/runny nose that prevented normal everyday activity, Grade 3 diarrhoea = greater than or equal to (≥) 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 3 fever = greater than (>) 39.0 degree Celsius (°C) (as defined by GSK Biologicals and the Chinese authorities), Grade 3 vomiting = ≥ 3 episodes of vomiting/day	
End point type	Primary
End point timeframe:	
Within the 8-day (Day 0-Day 7) follow-up period after each dose of HRV vaccine or placebo	

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	HRV Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	25		
Units: Subjects				
Grade 3 Cough; Dose 1 [N=25, 25]	0	0		
Grade 3 Diarrhoea; Dose 1 [N=25, 25]	2	1		
Grade 3 Irritability; Dose 1 [N=25, 25]	0	0		
Grade 3 Loss of appetite; Dose 1 [N=25, 25]	0	0		
Grade 3 temp (By GSK scale); Dose 1 [N=25, 25]	0	0		
Grade 3 temp (By Chinese scale); Dose 1 [N=25, 25]	0	0		
Grade 3 Vomiting; Dose 1 [N=25, 25]	1	0		
Grade 3 Cough; Dose 2 [N=23, 22]	0	0		
Grade 3 Diarrhoea; Dose 2 [N=23, 22]	1	1		
Grade 3 Irritability; Dose 2 [N=23, 22]	0	0		
Grade 3 Loss of appetite; Dose 2 [N=23, 22]	0	0		
Grade 3 temp (By GSK scale); Dose 2 [N=23, 22]	0	0		
Grade 3 temp (By Chinese scale); Dose 2 [N=23, 22]	0	0		

Grade 3 Vomiting; Dose 2 [N=23, 22]	1	0		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Assessed solicited general symptoms were cough, diarrhoea, irritability, loss of appetite, fever (By GSK scale and Chinese scale) and vomiting. Any = Incidence of any general symptom regardless of intensity grade or relationship to vaccination. Related = symptom assessed by the investigator as related to the vaccination. Any fever = 37.1 °C (as defined by the Chinese authorities) or 37.5°C (as defined by GSK Biologicals).

End point type	Secondary

End point timeframe:

Within the 8-day (Day 0-Day 7) follow-up period after each dose of HRV vaccine or placebo.

End point values	HRV Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	25		
Units: Subjects				
Any Cough; Dose 1 [N=25, 25]	3	5		
Related Cough; Dose 1 [N=25, 25]	0	0		
Any Diarrhoea; Dose 1 [N=25, 25]	4	2		
Related Diarrhoea; Dose 1 [N=25, 25]	0	1		
Any Irritability; Dose 1 [N=25, 25]	5	6		
Related Irritability; Dose 1 [N=25, 25]	0	0		
Any Loss of appetite; Dose 1 [N=25, 25]	3	5		
Related Loss of appetite; Dose 1 [N=25, 25]	0	0		
Any temperature (By GSK scale); Dose 1 [N=25, 25]	1	0		
Related temp (By GSK scale); Dose 1 [N=25, 25]	0	0		
Any temp (By Chinese scale); Dose 1 [N=25, 25]	1	2		
Related temp (By Chinese scale); Dose 1 [N=25, 25]	0	0		
Any Vomiting; Dose 1 [N=25, 25]	2	1		
Related Vomiting; Dose 1 [N=25, 25]	1	0		
Any Cough; Dose 2 [N=23, 22]	3	4		
Related Cough; Dose 2 [N=23, 22]	0	0		
Any Diarrhoea; Dose 2 [N=23, 22]	4	4		
Related Diarrhoea; Dose 2 [N=23, 22]	2	1		

Any Irritability; Dose 2 [N=23, 22]	1	5		
Related Irritability; Dose 2 [N=23, 22]	0	2		
Any Loss of appetite; Dose 2 [N=23, 22]	2	5		
Related Loss of appetite; Dose 2 [N=23, 22]	0	1		
Any temp (By GSK scale); Dose 2 [N=23, 22]	0	3		
Related temp (By GSK scale); Dose 2 [N=23, 22]	0	1		
Any temp (By Chinese scale); Dose 2 [N=23, 22]	3	6		
Related temp (By Chinese scale); Dose 2 [N=23, 22]	1	3		
Any Vomiting; Dose 2 [N=23, 22]	1	1		
Related Vomiting; Dose 2 [N=23, 22]	1	0		

Statistical analyses

No statistical analyses for this end point

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

End point title	Numbers 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. Also 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:

Within the 31-day (Day 0-Day 30) follow-up after any dose of HRV vaccine or placebo

End point values	HRV Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	25		
Units: Subjects				
any AE(s)	6	3		

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 medical occurrences that result in death, are life threatening, require hospitalization or prolongation of hospitalization or result in disability/incapacity.

End point type	Secondary

End point timeframe:

Throughout the study period (Day 0 up to Month 2).

End point values	HRV Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	25		
Units: Subjects				
Any SAE(s)	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-rotavirus IgA antibody concentration above the cut-off value

End point title	Number of subjects with anti-rotavirus IgA antibody concentration above the cut-off value

End point description:

The cut-off value for anti-rotavirus IgA antibody concentration was ≥ 20 U/mL

End point type	Secondary

End point timeframe:

At Day 0 and Month 2

End point values	HRV Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	17		
Units: Subjects				
Anti-RV.IgA; Day 0	0	0		
Anti-RV.IgA; Month 2	13	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum rotavirus immunoglobulin A (IgA) antibody concentrations

End point title	Serum rotavirus immunoglobulin A (IgA) antibody concentrations

End point description:

Concentrations are given as geometric mean concentrations (GMC) for anti-rotavirus IgA antibodies. Seroconverted subject is defined as a subject with appearance of anti-rotavirus (RV) IgA antibody concentration ≥ 20 units (U)/millilitre (mL) in subjects initially (i.e. prior to the first dose of HRV vaccine or placebo) seronegative for anti-RV IgA antibody). None of the subjects in the Placebo Group had seroconverted.

End point type	Secondary

End point timeframe:

At Day 0 and Month 2

End point values	HRV Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	17		
Units: U/mL				
geometric mean (confidence interval 95%)				
Anti-RV.IgA; Day 0	0 (99.8 to 746)	0 (0 to 0)		
Anti-RV.IgA; Month 2	272.8 (0 to 0)	0 (0 to 0)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with RV in stool samples (shedding)

End point title	Number of subjects with RV in stool samples (shedding)

End point description:

End point type	Secondary

End point timeframe:

At Day 0, Day 7 and Day 15 after each HRV vaccine or placebo dose and one month post-Dose 2 (Month 2)

End point values	HRV Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	17		
Units: Subjects				
Dose 1; Day 0	0	0		
Dose 1; Day 7	2	0		
Dose 1; Day 15	0	0		
Dose 2; Day 0	0	0		
Dose 2; Day 7	0	0		
Dose 2; Day 15	0	0		
Month 2; Day 0	0	1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited general symptom during the 8-day (Days 0-7) post-vaccination period; Unsolicited AEs within the 31-day (Days 0-30) follow-up after vaccination and SAEs during the entire study period (Day 0 to Month 2)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.0

Reporting groups

Reporting group title	HRV Group

Reporting group description:

Subjects received 2 oral doses of GlaxoSmithKline (GSK) Biologicals' oral live attenuated liquid human rotavirus (HRV)HRV vaccine according to a 0, 1 month schedule

Reporting group title	Placebo Group

Reporting group description:

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

Serious adverse events	HRV Group	Placebo Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 25 (4.00%)	0 / 25 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Congenital, familial and genetic disorders			
Heart disease congenital			
subjects affected / exposed	1 / 25 (4.00%)	0 / 25 (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			
Bronchopneumonia			
subjects affected / exposed	1 / 25 (4.00%)	0 / 25 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	HRV Group	Placebo Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 25 (20.00%)	6 / 25 (24.00%)	
General disorders and administration site conditions			
Irritability; Dose 1			
subjects affected / exposed	5 / 25 (20.00%)	6 / 25 (24.00%)	
occurrences (all)	5	6	
Loss of appetite; Dose 1			
subjects affected / exposed	3 / 25 (12.00%)	5 / 25 (20.00%)	
occurrences (all)	3	5	
Fever By Chinese scale; Dose 1			
subjects affected / exposed	1 / 25 (4.00%)	2 / 25 (8.00%)	
occurrences (all)	1	2	
Vomiting; Dose 1			
subjects affected / exposed	2 / 25 (8.00%)	1 / 25 (4.00%)	
occurrences (all)	2	1	
Diarrhoea; Dose 2			
subjects affected / exposed[1]	4 / 23 (17.39%)	4 / 22 (18.18%)	
occurrences (all)	4	4	
Irritability; Dose 2			
subjects affected / exposed[2]	1 / 23 (4.35%)	5 / 22 (22.73%)	
occurrences (all)	1	5	
Loss of appetite; Dose 2			
subjects affected / exposed[3]	2 / 23 (8.70%)	5 / 22 (22.73%)	
occurrences (all)	2	5	
Fever By GSK scale; Dose 2			
subjects affected / exposed[4]	0 / 23 (0.00%)	3 / 22 (13.64%)	
occurrences (all)	0	3	
Fever By Chinese scale; Dose 2			
subjects affected / exposed[5]	3 / 23 (13.04%)	6 / 22 (27.27%)	
occurrences (all)	3	6	
Gastrointestinal disorders			
Diarrhoea; Dose 1			
subjects affected / exposed	4 / 25 (16.00%)	2 / 25 (8.00%)	
occurrences (all)	4	2	
Respiratory, thoracic and mediastinal disorders			

Cough; Dose 1			
subjects affected / exposed	3 / 25 (12.00%)	5 / 25 (20.00%)	
occurrences (all)	3	5	
Cough; Dose 2			
subjects affected / exposed[6]	3 / 23 (13.04%)	4 / 22 (18.18%)	
occurrences (all)	3	4	
Infections and infestations			
Nasopharyngitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	4 / 25 (16.00%)	3 / 25 (12.00%)	
occurrences (all)	4	3	

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).

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