Clinical trial results:
A phase II, double-blind, randomized, placebo-controlled study to assess the safety, reactogenicity and immunogenicity of three doses of GlaxoSmithKline (GSK) Biologicals' oral live attenuated human rotavirus (HRV) vaccine (RIX4414 at 10 Exp 6.5 CCID50) administered to human immunodeficiency virus (HIV) infected infants at 6, 10 and 14 weeks of age in South Africa.

Summary

EudraCT number	2015-001484-39
Trial protocol	Outside EU/EEA
Global end of trial date	13 February 2008

Results information

Result version number	v2 (current)
This version publication date	15 November 2020
First version publication date	19 July 2015
Version creation reason	• Correction of full data set Results have been amended to account for consistency with other registries.

Trial information

Trial identification

Sponsor protocol code	444563/022

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00263666
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	24 June 2008
Is this the analysis of the primary completion data?	Yes
Primary completion date	07 February 2008
Global end of trial reached?	Yes
Global end of trial date	13 February 2008
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the safety and reactogenicity of 3 doses of GSK Biologicals' HRV vaccine versus placebo in HIV infected infants.

Protection of trial subjects:

The vaccinees 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 vaccines.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 March 2005
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	South Africa: 100
Worldwide total number of subjects	100
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)	100
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:

In case of discrepancy between the HIV results (DNA PCR positive, viral load negative), performed at the Screening
Visit (one week prior to first vaccination) the infants were not enrolled in the study.

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

Blinding implementation details:

The study was conducted in a double-blind manner. The parents/guardians of the subjects and the study personnel were unaware of the administered treatment (HRV vaccine or placebo).

Arms

Are arms mutually exclusive?	Yes
Arm title	Rotarix Group

Arm description:

Subjects received 3 doses of Rotarix vaccine co-administered with routine Tritanrix HepB Hib and Polio Sabin vaccines.

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

Dosage and administration details:

Oral vaccination

Investigational medicinal product name	Tritanrix-HB+Hib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Concomitant routine vaccination, IM administration

Investigational medicinal product name	PolioSabin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Oral administration, concomitant routine vaccination.

Arm title	Placebo Group

Arm description:

Subjects received 3 doses of placebo co-administered with routine Tritanrix HepB Hib and Polio Sabin vaccines.

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

Dosage and administration details:

Oral administration.

Investigational medicinal product name	Tritanrix-HB+Hib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Concomitant routine vaccination, IM administration.

Investigational medicinal product name	PolioSabin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder and solvent for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Oral administration, concomitant routine vaccination.

Number of subjects in period 1	Rotarix Group	Placebo Group
Started	50	50
Completed	43	39
Not completed	7	11
Consent withdrawn by subject	-	1
Adverse event, non-fatal	6	8
Lost to follow-up	1	2

Baseline characteristics

Reporting groups	
Reporting group title	Rotarix Group
Reporting group description:	
Subjects received 3 doses of Rotarix vaccine co-administered with routine Tritanrix HepB Hib and Polio Sabin vaccines.	
Reporting group title	Placebo Group
Reporting group description:	
Subjects received 3 doses of placebo co-administered with routine Tritanrix HepB Hib and Polio Sabin vaccines.	

Reporting group values	Rotarix Group	Placebo Group	Total
Number of subjects	50	50	100
Age categorical Units: Subjects			
Age continuous Units: weeks			
arithmetic mean	7.1	6.9	
standard deviation	± 1.1	± 1.02	-
Gender categorical Units: Subjects			
Female	28	25	53
Male	22	25	47

End points

End points reporting groups

Reporting group title	Rotarix Group
Reporting group description:	
Subjects received 3 doses of Rotarix vaccine co-administered with routine Tritanrix HepB Hib and Polio Sabin vaccines.	
Reporting group title	Placebo Group
Reporting group description:	
Subjects received 3 doses of placebo co-administered with routine Tritanrix HepB Hib and Polio Sabin vaccines.	

Primary: 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[1]
End point description:	
Symptoms reported in the table include: Fever: temperature (axillary route) > 38.0 degree Celsius (°C); Diarrhea: ≥ 4 looser than normal stools/day; Vomiting: ≥ 2 episodes of vomiting/day.	
End point type	Primary
End point timeframe:	
Within the 15-day solicited follow-up period after any dose	

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: This outcome was descriptive; hence no statistical analyses were required.

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: Subjects				
Any symptom, Across Doses	26	28		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any unsolicited symptoms

End point title	Number of subjects reporting any unsolicited symptoms
End point description:	
An unsolicited symptom was any spontaneously reported untoward medical occurrence in a subject, temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.	
End point type	Secondary
End point timeframe:	
Within 30 days after any dose	

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: Subjects				
Any symptom	47	48		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any serious adverse events

End point title	Number of subjects reporting any serious adverse events

End point description:

A serious adverse event (SAE) is any untoward medical occurrence that: results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in disability/incapacity, is a congenital anomaly/birth defect in the offspring of a study subject, or may evolve into one of the outcomes listed above.

End point type	Secondary

End point timeframe:

Until 2 months after dose 3 (for subjects RV negative at Day 42 post-dose 3) or until end of RV shedding (for subjects who shed RV at Day 42 post-dose 3)

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: Subjects				
Any SAE(s)	17	12		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting each type of solicited symptom

End point title	Number of subjects reporting each type of solicited symptom

End point description:

Solicited symptoms included Cough, Diarrhea (3 or more looser than normal stools/day), Fever (axillary temperature ≥ 37.5°C), Irritability, Loss of appetite, and Vomiting.

End point type	Secondary

End point timeframe:

Within the 15-day solicited follow-up period after each dose

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: Subjects				
Cough, after dose 1 (N=50,50)	24	25		
Diarrhoea, after dose 1 (N=50,50)	8	8		
Fever, after dose 1 (N=50,50)	20	19		
Irritability, after dose 1 (N=50,50)	24	24		
Loss of appetite, after dose 1 (N=50,50)	18	19		
Vomiting, after dose 1 (N=50,50)	11	10		
Cough, after dose 2 (N=46,48)	18	19		
Diarrhoea, after dose 2 (N=46,48)	3	7		
Fever, after dose 2 (N=46,48)	15	12		
Irritability, after dose 2 (N=46,48)	20	19		
Loss of appetite, after dose 2 (N=46,48)	15	15		
Vomiting, after dose 2 (N=46,48)	9	10		
Cough, after dose 3 (N=45,44)	18	17		
Diarrhoea, after dose 3 (N=45,44)	7	4		
Fever, after dose 3 (N=45,44)	17	13		
Irritability, after dose 3 (N=45,44)	17	18		
Loss of appetite, after dose 3 (N=45,44)	10	12		
Vomiting, after dose 3 (N=45,44)	12	6		

Statistical analyses

No statistical analyses for this end point

Secondary: The number of subjects with no evidence of immunosuppression and moderate/severe suppresion, based on CD4+ absolute cell count and CD4+ percent

End point title	The number of subjects with no evidence of immunosuppression and moderate/severe suppresion, based on CD4+ absolute cell count and CD4+ percent

End point description:

Severe suppression: CD4+ cells/microliter (µl) < 750 and CD4+ percent < 15 percent (%); No evidence of suppression: CD4+ cells/µl ≥ 1500 and CD4+ percent ≥ 25%; Moderate suppression = all other CD4+ cell count and CD4+ % combinations.

End point type	Secondary

End point timeframe:

At the screening visit and 2 months after dose 3 (Visit 4)

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: Subjects				
Severe suppression at screening (n= 50, 50)	1	2		
Moderate suppression at screening (n= 50, 50)	12	15		
No suppression at screening (n= 50, 50)	37	33		
Severe suppression at Visit 4 (n= 43, 39)	11	7		
Moderate suppression at Visit 4 (n= 43, 39)	15	18		
No suppression at Visit 4 (n= 43, 39)	13	10		
Unknown at Visit 4 (n= 43, 39)	4	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Human immunodeficiency virus (HIV) Viral load

End point title	Human immunodeficiency virus (HIV) Viral load

End point description:

The HIV viral load was expressed as mean and standard deviation of the base-10 logarithm of HIV-1 ribonucleic acid (RNA) copies per milliliter (mL).

End point type	Secondary

End point timeframe:

At the screening visit and 2 months after dose 3

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: base-10 logarithm of copies/milliliter				
arithmetic mean (standard deviation)				
At screening (n= 50, 50)	5.7 (± 0.52)	5.7 (± 0.51)		
Two months after dose 3 (n= 43, 36)	5.6 (± 0.77)	5.7 (± 0.51)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects who seroconverted against rotavirus

End point title	Number of subjects who seroconverted against rotavirus

End point description:

A subject with anti-rotavirus Immunoglobulin (IgA) antibody concentration < 20 units/milliliter (U/mL) before vaccination and ≥ 20 U/mL after vaccination is considered as seroconverted.

End point type	Secondary

End point timeframe:

Two months after dose 3

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	22		
Units: Subjects	12	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with vaccine take

End point title	Number of subjects with vaccine take

End point description:

Vaccine take: appearance of serum IgA to rotavirus at a concentration of ≥ 20 U/ml or rotavirus shedding in any stool sample collected from the Screening Visit to 2 months after dose 3 for subjects initially negative for rotavirus.

End point type	Secondary

End point timeframe:

Two months after dose 3

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	22		
Units: Subjects	15	7		

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[2]

End point description:

Concentrations are given as geometric mean concentrations (GMC) for anti-rotavirus IgA antibodies.

End point type	Secondary

End point timeframe:

Two months after dose 3

Notes:

[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: In the Placebo Group, GMCs were all < 20 U/ml, hence values were not computed. Therefore, this outcome measure concerns subjects in Rotarix Group only.

End point values	Rotarix Group			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: U/ml				
geometric mean (confidence interval 95%)	75.5 (29.1 to 195.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-polyribosyl ribitol phosphate (PRP) antibody concentrations more than or equal to the cut-off value

End point title	Number of subjects with anti-polyribosyl ribitol phosphate (PRP) antibody concentrations more than or equal to the cut-off value

End point description:

Cut-off values for anti-PRP antibody concentrations were ≥ 0.15 and ≥ 1.0 microgram/milliliter (µg/mL).

End point type	Secondary

End point timeframe:

Two months after dose 3

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	24		
Units: Subjects				
≥ 0.15 µg/mL	20	23		
≥ 1 µg/mL	20	22		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Concentration for anti-PRP antibodies

End point title	Geometric Mean Concentration for anti-PRP antibodies

End point description:

Anti-PRP antibody concentrations are presented as geometric mean concentrations, expressed in

microgram/milliliter (µg/mL).

End point type	Secondary

End point timeframe:

Two months after dose 3

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	24		
Units: µg/mL				
geometric mean (confidence interval 95%)	4.641 (1.764 to 12.215)	4.865 (2.322 to 10.192)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-diphtheria and anti-tetanus toxoids antibody concentrations more than or equal to the cut-off value

End point title	Number of subjects with anti-diphtheria and anti-tetanus toxoids antibody concentrations more than or equal to the cut-off value

End point description:

The cut-off value was ≥ 0.1 International Units/milliliter (IU/mL).

End point type	Secondary

End point timeframe:

Two months after dose 3

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	25		
Units: Subjects				
Anti-diphtheria	19	19		
Anti-tetanus	23	24		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Concentration for anti-diphtheria and anti-tetanus toxoids antibodies

End point title	Geometric Mean Concentration for anti-diphtheria and anti-tetanus toxoids antibodies

End point description:

Anti-diphteria and anti-tetanus toxoids antibody concentrations are presented as geometric mean concentrations, expressed in international units/milliliter (IU/mL).

End point type	Secondary

End point timeframe:

Two months after dose 3

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	25		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-tetanus	1.457 (0.794 to 2.674)	1.035 (0.647 to 1.656)		
Anti-diphtheria	0.283 (0.167 to 0.481)	0.219 (0.143 to 0.337)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-hepatitis B (HBs) antibody concentrations more than or equal to the cut-off value

End point title	Number of subjects with anti-hepatitis B (HBs) antibody concentrations more than or equal to the cut-off value

End point description:

The cut-off value was ≥ 10 milli international units/milliliter (mIU/mL).

End point type	Secondary

End point timeframe:

Two months after dose 3

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	20		
Units: Subjects	15	11		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Concentration for anti-HBs antibodies

End point title	Geometric Mean Concentration for anti-HBs antibodies

End point description:

Anti-HBs antibody concentrations are presented as geometric mean concentrations, expressed in milli international units/milliliter (mIU/mL).

End point type	Secondary

End point timeframe:

Two months after dose 3

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	20		
Units: mIU/mL				
geometric mean (confidence interval 95%)	25.6 (14.3 to 45.8)	18.9 (9.9 to 36.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-Bordetella pertussis (BPT) antibody concentrations more than or equal to the cut-off value

End point title	Number of subjects with anti-Bordetella pertussis (BPT) antibody concentrations more than or equal to the cut-off value

End point description:

The cut-off value was ≥ 15 Enzyme Linked Immunosorbent Assay Unit/milliliter (EL.U/mL).

End point type	Secondary

End point timeframe:

Two months after dose 3

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	24		
Units: Subjects	19	14		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Concentration for anti-BPT antibodies

End point title	Geometric Mean Concentration for anti-BPT antibodies

End point description:

Anti-BPT antibody concentrations are presented as geometric mean concentrations, expressed in ELISA units/milliliter (EL.U/mL).

End point type	Secondary

End point timeframe:

Two months after dose 3

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	24		
Units: EL.U/mL				
geometric mean (confidence interval 95%)	28.8 (19.3 to 42.8)	18.1 (12.8 to 25.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with anti-polio types 1, 2 and 3 antibody titers more than or equal to the cut-off value

End point title	Number of subjects with anti-polio types 1, 2 and 3 antibody titers more than or equal to the cut-off value

End point description:

The cut-off value was ≥ 1:8. The lowest dilution at which serum samples were tested was 1:8, from which a test was considered positive.

End point type	Secondary

End point timeframe:

Two months after dose 3

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	24		
Units: Subjects				
Anti-polio type 1 (n= 25, 24)	19	15		
Anti-polio type 2 (n= 25, 24)	23	21		
Anti-polio type 3 (n= 25, 23)	18	15		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Titer for anti-polio types 1, 2 and 3 antibodies

End point title	Geometric Mean Titer for anti-polio types 1, 2 and 3 antibodies

End point description:

Anti-polio types 1, 2 and 3 antibody titers are presented as geometric mean titers.

End point type	Secondary

End point timeframe:

Two months after dose 3

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	24		
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-polio 1 (n= 25, 24)	90.5 (36.4 to 225.3)	53 (19.4 to 144.5)		
Anti-polio 2 (n= 25, 24)	142.6 (60.8 to 334.2)	252.4 (91.2 to 698.7)		
Anti-polio 3 (n= 25, 23)	44.7 (19.2 to 104.2)	66 (22.6 to 192.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Rotavirus antigen excretion in stool samples

End point title	Rotavirus antigen excretion in stool samples

End point description:

Number of subjects with rotavirus detected by Enzyme Linked Immunosorbent Assay (ELISA) in stool samples collected from Dose 1 until study end.

End point type	Secondary

End point timeframe:

At day of each vaccination and at planned days following each vaccine dose until 2 months after dose 3 or until end of RV shedding

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	25	25		
Units: Subjects	11	5		

Statistical analyses

No statistical analyses for this end point

Secondary: Rotavirus in diarrheal stool samples

End point title	Rotavirus in diarrheal stool samples

End point description:

Number of subjects reporting at least one rotavirus (vaccine strain or wild type rotavirus) gastroenteritis episode.

End point type	Secondary

End point timeframe:

From Dose 1 until 2 months after dose 3 or until end of RV shedding

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: Subjects				
Subjects with at least 1 GE episode	4	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Enteric pathogens identification

End point title	Enteric pathogens identification

End point description:

Number of subjects reporting at least one episode of gastroenteritis (GE) classified by enteric pathogen tests results.

End point type	Secondary

End point timeframe:

From Dose 1 until 2 months after dose 3 or until end of RV shedding

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	29	34		
Units: Subjects				
Campylobacter, negative	18	24		
Campylobacter, positive	0	0		
Campylobacter, unknown	11	10		
E. histolytica, negative	18	24		
E. histolytica, positive	0	0		
E. histolytica, unknown	11	10		
Salmonella, negative	17	24		
Salmonella, positive	1	0		
Salmonella, unknown	11	10		
Sto Epec, negative	3	5		
Sto Epec, positive	0	0		

Sto Epec, unknown	26	29		
Sto G.Lamblia, negative	18	24		
Sto G.Lamblia, positive	0	0		
Sto G.Lamblia, unknown	11	10		
Sto Shigella, negative	18	24		
Sto Shigella, positive	0	0		
Sto Shigella, unknown	11	10		
Sto Yersinia, negative	18	24		
Sto Yersinia, positive	0	0		
Sto Yersinia, unknown	11	10		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with the RV in stool samples

End point title	Number of subjects with the RV in stool samples

End point description:

Number of subjects with presence of RV in stool samples (shedding) collected at pre-determined time points by RV type (Yes, No, Mixed type = G1V+G1WT+G2+G3+P4+P8V+P8WT and results not available [NA]).

End point type	Secondary

End point timeframe:

From Dose 1 until post Dose 3

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	7		
Units: Subjects				
Dose 1 (Day 7; Yes) (N=9, 1)	7	0		
Dose 1 (Day 7; No) (N=9,1)	0	0		
Dose 1 (Day 7; NA) (N=9,1)	2	1		
Dose 1 (Day 14; Yes) (N=4,2)	0	0		
Dose 1 (Day 14; No) (N=4,2)	0	1		
Dose 1 (Day 14; Mixed) (N=4,2)	0	1		
Dose 1 (Day 14; NA) (N=4,2)	4	0		
Dose 1 (Day 21; Yes) (N=5,1)	1	0		
Dose 1 (Day 21; No) (N=5,1)	0	1		
Dose 1 (Day 21; NA) (N=5,1)	4	0		
Dose 2 (Day 7; Yes) (N=0,1)	0	0		
Dose 2 (Day 7; No) (N=0,1)	0	1		
Dose 2 (Day 7; NA) (N=0,1)	0	0		
Dose 2 (Day 14; Yes) (N=1,0)	0	0		
Dose 2 (Day 14; No) (N=1,0)	0	0		
Dose 2 (Day 14; NA) (N=1,0)	1	0		
Dose 2 (Day 21; Yes) (N=2,0)	0	0		
Dose 2 (Day 21; No) (N=2,0)	0	0		

Dose 2 (Day 21; NA) (N=2,0)	2	0		
Dose 3 (Day 7; Yes) (N=1,1)	0	0		
Dose 3 (Day 7; No) (N=1,1)	0	1		
Dose 3 (Day 7; NA) (N=1,1)	1	0		
Dose 3 (Day 14; Yes) (N=2,0)	2	0		
Dose 3 (Day 14; No) (N=2,0)	0	0		
Dose 3 (Day 14; NA) (N=2,0)	0	0		
Dose 3 (Day 42; Yes) (N=1,1)	0	0		
Dose 3 (Day 42; No) (N=1,1)	0	0		
Dose 3 (Day 42; NA) (N=1,1)	1	1		
Post Dose 3 (Day 0; Yes) (N=1,0)	0	0		
Post Dose 3 (Day 0; No) (N=1,0)	0	0		
Post Dose 3 (Day 0; NA) (N=1,0)	1	0		
Overall total (overall total; Yes) (N=26,7)	10	0		
Overall total (overall total; No) (N=26,7)	0	4		
Overall total (overall total;Mixed type) (N=26,7)	0	1		
Overall total (overall total; NA) (N=26,7)	16	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Rotavirus vaccine strain identification

End point title	Rotavirus vaccine strain identification

End point description:

Number of gastroenteritis (GE) episodes classified by rotavirus vaccine strain/serotype. Unknown: These samples were typed post hoc and found "G1P8" vaccine type for one subject in HRV group, "G3P8" and "G2P4" for subjects in placebo group.

End point type	Secondary

End point timeframe:

From dose 1 until 2 months after dose 3 or until end of RV shedding

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	50	50		
Units: Number of episodes				
number (not applicable)				
G1WT+P8WT	2	0		
G2+P4	0	1		
G3+P8	0	1		
GX+P6	1	0		
Unknown	1	2		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited general symptoms during the 15-day (Days 0-14) post-vaccination period following each dose and across doses, unsolicited AEs within 31 days (Days 0-30) after any vaccination and SAEs throughout the study period.

Adverse event reporting additional description:

The occurrence of reported AEs (all/related) was not available and encoded as equal to the number of subjects affected.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	11.0

Reporting groups

Reporting group title	Rotarix Group

Reporting group description:

Subjects received 3 doses of Rotarix vaccine co-administered with routine Tritanrix HepB Hib and Polio Sabin vaccines.

Reporting group title	Placebo Group

Reporting group description:

Subjects received 3 doses of placebo co-administered with routine Tritanrix HepB Hib and Polio Sabin vaccines.

Serious adverse events	Rotarix Group	Placebo Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	17 / 50 (34.00%)	12 / 50 (24.00%)	
number of deaths (all causes)	6	9	
number of deaths resulting from adverse events	6	9	
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	1 / 50 (2.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Sudden infant death syndrome			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Eye disorders			
Conjunctivitis			

subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Ileus paralytic			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Respiratory, thoracic and mediastinal disorders			
Epistaxis			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonia aspiration			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Respiratory failure			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			

subjects affected / exposed	7 / 50 (14.00%)	4 / 50 (8.00%)	
occurrences causally related to treatment / all	0 / 7	0 / 4	
deaths causally related to treatment / all	1 / 2	3 / 4	
Lobar pneumonia			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumocystis jiroveci pneumonia			
subjects affected / exposed	2 / 50 (4.00%)	2 / 50 (4.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	1 / 1	0 / 1	
Pneumonia			
subjects affected / exposed	1 / 50 (2.00%)	3 / 50 (6.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Lymph node tuberculosis			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary tuberculosis			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculosis			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Dysentery			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			

subjects affected / exposed	6 / 50 (12.00%)	3 / 50 (6.00%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	1 / 1	0 / 0	
HIV infection			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Meningitis			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral candidiasis			
subjects affected / exposed	1 / 50 (2.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
subjects affected / exposed	2 / 50 (4.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	3 / 50 (6.00%)	0 / 50 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	2 / 2	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	2 / 50 (4.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Electrolyte imbalance			
subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Marasmus			

subjects affected / exposed	0 / 50 (0.00%)	1 / 50 (2.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

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	48 / 50 (96.00%)	47 / 50 (94.00%)	
Investigations			
Weight decreased			
subjects affected / exposed	1 / 50 (2.00%)	4 / 50 (8.00%)	
occurrences (all)	1	4	
Blood and lymphatic system disorders			
Lymphadenopathy			
subjects affected / exposed	5 / 50 (10.00%)	3 / 50 (6.00%)	
occurrences (all)	5	3	
Splenomegaly			
subjects affected / exposed	2 / 50 (4.00%)	4 / 50 (8.00%)	
occurrences (all)	2	4	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	3 / 50 (6.00%)	6 / 50 (12.00%)	
occurrences (all)	3	6	
Cough (solicited)			
alternative assessment type: Systematic			
subjects affected / exposed	35 / 50 (70.00%)	31 / 50 (62.00%)	
occurrences (all)	35	31	
Diarrhoea			
alternative assessment type: Systematic			
subjects affected / exposed	16 / 50 (32.00%)	16 / 50 (32.00%)	
occurrences (all)	16	16	
Fever			
alternative assessment type: Systematic			

subjects affected / exposed	30 / 50 (60.00%)	28 / 50 (56.00%)	
occurrences (all)	30	28	
Irritability			
alternative assessment type: Systematic			
subjects affected / exposed	31 / 50 (62.00%)	28 / 50 (56.00%)	
occurrences (all)	31	28	
Loss of appetite			
alternative assessment type: Systematic			
subjects affected / exposed	23 / 50 (46.00%)	23 / 50 (46.00%)	
occurrences (all)	23	23	
Vomiting (solicited)			
alternative assessment type: Systematic			
subjects affected / exposed	19 / 50 (38.00%)	15 / 50 (30.00%)	
occurrences (all)	19	15	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	1 / 50 (2.00%)	3 / 50 (6.00%)	
occurrences (all)	1	3	
Vomiting			
subjects affected / exposed	1 / 50 (2.00%)	5 / 50 (10.00%)	
occurrences (all)	1	5	
Abdominal pain			
subjects affected / exposed	2 / 50 (4.00%)	3 / 50 (6.00%)	
occurrences (all)	2	3	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 50 (2.00%)	5 / 50 (10.00%)	
occurrences (all)	1	5	
Nasal congestion			
subjects affected / exposed	4 / 50 (8.00%)	4 / 50 (8.00%)	
occurrences (all)	4	4	
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	4 / 50 (8.00%)	4 / 50 (8.00%)	
occurrences (all)	4	4	
Dermatitis diaper			

subjects affected / exposed	5 / 50 (10.00%)	4 / 50 (8.00%)	
occurrences (all)	5	4	
Eczema			
subjects affected / exposed	2 / 50 (4.00%)	8 / 50 (16.00%)	
occurrences (all)	2	8	
Rash			
subjects affected / exposed	4 / 50 (8.00%)	2 / 50 (4.00%)	
occurrences (all)	4	2	
Rash papular			
subjects affected / exposed	0 / 50 (0.00%)	3 / 50 (6.00%)	
occurrences (all)	0	3	
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	18 / 50 (36.00%)	14 / 50 (28.00%)	
occurrences (all)	18	14	
Pulmonary tuberculosis			
subjects affected / exposed	2 / 50 (4.00%)	4 / 50 (8.00%)	
occurrences (all)	2	4	
Influenza			
subjects affected / exposed	6 / 50 (12.00%)	0 / 50 (0.00%)	
occurrences (all)	6	0	
Pharyngitis			
subjects affected / exposed	1 / 50 (2.00%)	3 / 50 (6.00%)	
occurrences (all)	1	3	
Bronchopneumonia			
subjects affected / exposed	11 / 50 (22.00%)	6 / 50 (12.00%)	
occurrences (all)	11	6	
Gastroenteritis			
subjects affected / exposed	9 / 50 (18.00%)	9 / 50 (18.00%)	
occurrences (all)	9	9	
Oral candidiasis			
subjects affected / exposed	15 / 50 (30.00%)	19 / 50 (38.00%)	
occurrences (all)	15	19	
Otitis media			
subjects affected / exposed	4 / 50 (8.00%)	6 / 50 (12.00%)	
occurrences (all)	4	6	

Sepsis subjects affected / exposed occurrences (all)	3 / 50 (6.00%) 3	0 / 50 (0.00%) 0	
Metabolism and nutrition disorders Dehydration subjects affected / exposed occurrences (all)	3 / 50 (6.00%) 3	0 / 50 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 November 2004	In response to comments from the Ethical committee of the WHO (SCRIHS), the following implementations were performed: • The study sites were described. Information on the pool from which subjects will be recruited as well as on the screening process was added. • The diagnostic plans for fatalities and their follow-up were described. • An Independent Data Monitoring Committee (IDMC) who is monitoring the safety aspects of GSK Biologicals HRV vaccine clinical development, will review each SAE/IS case and may recommend a clinical study hold in case of safety concern. • Since the study sites have different recommendations for the mother with regard to feeding the subjects, it was decided to record information on feeding practices. This will allow to explore any influence of feeding practice on vaccine take. • The safety data obtained with GSK Biologicals HRV vaccine since the finalization of the original protocol (dated 29 July 2003) were updated. • Other minor modifications (e.g. update of laboratory names and commercial kit versions for HIV testing; update to reflect the current processes to be followed for surgical specimens in case of IS) and administrative changes were made.
19 August 2005	• To update the safety data obtained with GSK Biologicals' HRV vaccine since the finalization of the original protocol and amendment 1 (dated 5 November 2004). • To update the Regulatory reporting requirements for serious adverse events according to latest version of GSK Biologicals' standard protocol. • Describe that GSK facilitate access to anti retroviral (ARV) treatment centers for subjects who develop clinical symptoms or have CD4 count below 20%. • To add the more recent description of immunologic and clinical categories of HIV disease: according to the WHO and Republic of South Africa (RSA) National guidelines. • To reflect other minor modifications (e.g. update of some laboratory tests and names of lab). • To reflect the IDMC's request to evaluate the presence of persistent or recurrent shedding of rotavirus at the final visit.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported