Clinical trial results:
A phase IIIb open study to assess the long-term efficacy and safety of GlaxoSmithKline (GSK) Biologicals' oral live attenuated human rotavirus (HRV) vaccine approximately three years after vaccination in healthy infants aged 6-12 weeks at the time of first vaccination in the Rota-036 study (102247) in Finland

Summary

EudraCT number	2006-006552-36
Trial protocol	FI
Global end of trial date	08 August 2007

Results information

Result version number	v2 (current)
This version publication date	02 June 2023
First version publication date	23 July 2016
Version creation reason	• Correction of full data set Correction of full data set and alignment between registries.

Trial information

Trial identification

Sponsor protocol code	109810

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00420316
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	08 August 2007
Is this the analysis of the primary completion data?	Yes
Primary completion date	08 August 2007
Global end of trial reached?	Yes
Global end of trial date	08 August 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

•To assess the efficacy of GSK Biologicals' HRV vaccine with respect to any rotavirus gastroenteritis (RV GE) episodes caused by the circulating wild-type RV strains during the follow-up period.

Protection of trial subjects:

All subjects in the primary study (2004-001175-19) were supervised for 30 minutes after vaccination/product administration with appropriate medical treatment readily available. Vaccines/products were administered by qualified and trained personnel. Vaccines/products were administered only to eligible subjects that had no contraindications to any components of the vaccines/products.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 February 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	Finland: 1613
Worldwide total number of subjects	1613
EEA total number of subjects	1613

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)	1613
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	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Rotarix Group

Arm description:

Healthy children between and including 6 to 12 weeks of age at the time of first vaccination, who received two powdered oral doses of Rotarix vaccine in the Rota-036 primary vaccination study (102247), were subsequently followed-up for 6 months during their third year of age, in scope of the present study.

Arm type	Experimental
Investigational medicinal product name	Rotarix
Investigational medicinal product code	
Other name	Live attenuated human rotavirus (HRV) vaccine
Pharmaceutical forms	Powder for oral solution
Routes of administration	Oral use

Dosage and administration details:

Oral administration of 2 doses of Rotarix vaccine in the primary study. No vaccine was administered during this extension study.

Arm title	Placebo Group

Arm description:

Healthy children between and including 6 to 12 weeks of age at the time of first vaccination, who received two liquid oral doses of placebo in the Rota-036 primary vaccination study (102247), were subsequently followed-up for 6 months during their third year of age, in scope of the present study.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	Live attenuated human rotavirus (HRV) vaccine
Pharmaceutical forms	Oral liquid
Routes of administration	Oral use

Dosage and administration details:

Oral administration of 2 doses of placebo in the primary study. No vaccine was administered during this extension study.

Number of subjects in period 1	Rotarix Group	Placebo Group
Started	1082	531
Completed	1070	522
Not completed	12	9
Consent withdrawn by subject	-	1
Lost to follow-up	12	8

Baseline characteristics

Reporting groups	
Reporting group title	Rotarix Group
Reporting group description:	
Healthy children between and including 6 to 12 weeks of age at the time of first vaccination, who received two powdered oral doses of Rotarix vaccine in the Rota-036 primary vaccination study (102247), were subsequently followed-up for 6 months during their third year of age, in scope of the present study.	
Reporting group title	Placebo Group
Reporting group description:	
Healthy children between and including 6 to 12 weeks of age at the time of first vaccination, who received two liquid oral doses of placebo in the Rota-036 primary vaccination study (102247), were subsequently followed-up for 6 months during their third year of age, in scope of the present study.	

Reporting group values	Rotarix Group	Placebo Group	Total
Number of subjects	1082	531	1613
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)	1082	531	1613
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: months			
arithmetic mean	31.2	31.3	
standard deviation	± 1.12	± 1.19	-
Gender categorical			
Units: Subjects			
Female	510	266	776
Male	572	265	837

End points

End points reporting groups

Reporting group title	Rotarix Group

Reporting group description:

Healthy children between and including 6 to 12 weeks of age at the time of first vaccination, who received two powdered oral doses of Rotarix vaccine in the Rota-036 primary vaccination study (102247), were subsequently followed-up for 6 months during their third year of age, in scope of the present study.

Reporting group title	Placebo Group

Reporting group description:

Healthy children between and including 6 to 12 weeks of age at the time of first vaccination, who received two liquid oral doses of placebo in the Rota-036 primary vaccination study (102247), were subsequently followed-up for 6 months during their third year of age, in scope of the present study.

Primary: Number of subjects with any rotavirus gastroenteritis (RVGE)

End point title	Number of subjects with any rotavirus gastroenteritis (RVGE)

End point description:

Occurence of any rotavirus gastroenteritis caused by the circulating wild-type rotavirus strain was assessed in terms of number of subjects experiencing diarrhoea with or without vomiting. Two occurrences of diarrhoea were classified as separate episodes if there were 5 or more diarrhoea-free days between the episodes.

End point type	Primary

End point timeframe:

During the study period for the long-term follow-up (i.e. 6 months)

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1065	525		
Units: Subjects	4	3		

Statistical analyses

Statistical analysis title	Vaccine efficacy with respect to any RVGE

Statistical analysis description:

Vaccine efficacy with respect to any rotavirus gastroenteritis (RVGE) caused by the circulating wild-type rotavirus strain. Vaccine efficacy (VE) was defined as the percent reduction in the frequency of the relevant outcome variable in vaccinated subjects compared with those subjects who received placebo.

Comparison groups	Rotarix Group v Placebo Group
Number of subjects included in analysis	1590
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.691
Method	Fisher exact
Parameter estimate	Percent reduction
Point estimate	34.3

Confidence interval	
level	95 %
sides	2-sided
lower limit	-348.7
upper limit	88.9

Secondary: Number of subjects with severe rotavirus gastroenteritis (RVGE)

End point title	Number of subjects with severe rotavirus gastroenteritis (RVGE)

End point description:

Number of rotavirus gastroenteritis episodes caused by the wild-type rotavirus strain and reported during the efficacy period, were presented by severity, using the Vesikari scale. The assessment of intensity of GE episodes was done using the 20-point Vesikari scale, according to which episodes with scores greater than or equal to (≥)11 were labeled as severe.

End point type	Secondary

End point timeframe:

During the study period for the long-term follow-up (i.e. 6 months)

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1065	525		
Units: Subjects	1	1		

Statistical analyses

Statistical analysis title	Vaccine efficacy with respect to severe RVGE

Statistical analysis description:

Vaccine efficacy with respect to severe rotavirus gastroenteritis (RVGE) caused by the circulating wild-type rotavirus strain. Vaccine efficacy (VE) was defined as the percent reduction in the frequency of the relevant outcome variable in vaccinated subjects compared with those subjects who received placebo.

Comparison groups	Rotarix Group v Placebo Group
Number of subjects included in analysis	1590
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.551
Method	Fisher exact
Parameter estimate	Percent reduction
Point estimate	50.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3769.6
upper limit	99.4

Secondary: Number of subjects with any rotavirus gastroenteritis (RVGE) with G1 serotype

End point title	Number of subjects with any rotavirus gastroenteritis (RVGE) with G1 serotype

End point description:

Occurence of any rotavirus gastroenteritis caused by the circulating wild-type rotavirus strain was assessed in terms of number of subjects experiencing diarrhoea with or without vomiting. Two occurrences of diarrhoea were classified as separate episodes if there were 5 or more diarrhoea-free days between the episodes. Only GE episodes in which wild-type RV strain of G1 serotype was identified in a stool specimen, were included in the efficacy analysis.

End point type	Secondary

End point timeframe:

During the study period for the long-term follow-up (i.e. 6 months)

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1065	525		
Units: Subjects				
Any RVGE	0	2		

Statistical analyses

Statistical analysis title	Vaccine efficacy with respect to any RVGE

Statistical analysis description:

Vaccine efficacy with respect to any rotavirus gastroenteritis (RVGE) caused by the wild-type rotavirus strain of serotype G1.
Vaccine efficacy (VE) was defined as the percent reduction in the frequency of the relevant outcome variable in vaccinated subjects compared with those subjects who received placebo.

Comparison groups	Rotarix Group v Placebo Group
Number of subjects included in analysis	1590
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.109
Method	Fisher exact
Parameter estimate	Percent reduction
Point estimate	100
Confidence interval	
level	95 %
sides	2-sided
lower limit	-162.5
upper limit	100

Secondary: Number of subjects with severe rotavirus gastroenteritis (RVGE) with G1 serotype

End point title	Number of subjects with severe rotavirus gastroenteritis (RVGE) with G1 serotype

End point description:

Number of rotavirus gastroenteritis episodes caused by the wild-type rotavirus strain of serotype G1 and reported during the efficacy period, were presented by severity, using the Vesikari scale. The assessment of intensity of GE episodes was done using the 20-point Vesikari scale, according to which episodes with scores ≥11 were labeled as severe.

End point type	Secondary

End point timeframe:

During the study period for the long-term follow-up (i.e. 6 months)

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1065	525		
Units: Subjects				
Severe RVGE	0	1		

Statistical analyses

Statistical analysis title	Vaccine efficacy with respect to severe RVGE

Statistical analysis description:

Vaccine efficacy with respect to severe rotavirus gastroenteritis (RVGE) caused by the wild-type rotavirus strain of serotype G1. Vaccine efficacy (VE) was defined as the percent reduction in the frequency of the relevant outcome variable in vaccinated subjects compared with those subjects who received placebo.

Comparison groups	Rotarix Group v Placebo Group
Number of subjects included in analysis	1590
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.33
Method	Fisher exact
Parameter estimate	Percent reduction
Point estimate	100
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1822.5
upper limit	100

Secondary: Number of subjects with any rotavirus gastroenteritis (RVGE) with non-G1 serotype

End point title	Number of subjects with any rotavirus gastroenteritis (RVGE)

	with non-G1 serotype

End point description:

Occurence of any rotavirus gastroenteritis caused by the circulating wild-type rotavirus strain of non-G1 serotype was assessed in terms of number of subjects experiencing diarrhoea with or without vomiting. Two occurrences of diarrhoea were classified as separate episodes if there were 5 or more diarrhoea-free days between the episodes.

End point type	Secondary

End point timeframe:

During the study period for the long-term follow-up (i.e. 6 months)

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1065	525		
Units: Subjects				
Any RVGE	4	1		

Statistical analyses

Statistical analysis title	Vaccine efficacy with respect to any RVGE

Statistical analysis description:

Vaccine efficacy with respect to any rotavirus gastroenteritis (RVGE) caused by the wild-type rotavirus strain of non-G1 serotype. Vaccine efficacy (VE) was defined as the percent reduction in the frequency of the relevant outcome variable in vaccinated subjects compared with those subjects who received placebo.

Comparison groups	Rotarix Group v Placebo Group
Number of subjects included in analysis	1590
Analysis specification	Pre-specified
Analysis type	other
P-value	= 1
Method	Fisher exact
Parameter estimate	Percent reduction
Point estimate	-97.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9610.8
upper limit	80.5

Secondary: Number of subjects with severe rotavirus gastroenteritis (RVGE) with non-G1 serotype

End point title	Number of subjects with severe rotavirus gastroenteritis (RVGE) with non-G1 serotype

End point description:

Number of rotavirus gastroenteritis episodes caused by the wild-type rotavirus strain of non-G1 serotype and reported during the efficacy period, were presented by severity, using the Vesikari scale. The assessment of intensity of GE episodes was done using the 20-point Vesikari scale, according to which episodes with scores ≥ 11 were labeled as severe.

End point type	Secondary

End point timeframe:

During the study period for the long-term follow-up (i.e. 6 months)

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1065	525		
Units: Subjects				
Severe RVGE	1	0		

Statistical analyses

Statistical analysis title	Vaccine efficacy with respect to severe RVGE

Statistical analysis description:

Vaccine efficacy with respect to severe rotavirus gastroenteritis (RVGE) caused by the wild-type rotavirus strain of non-G1 serotype. Vaccine efficacy (VE) was defined as the percent reduction in the frequency of the relevant outcome variable in vaccinated subjects compared with those subjects who received placebo.

Comparison groups	Placebo Group v Rotarix Group
Number of subjects included in analysis	1590
Analysis specification	Pre-specified
Analysis type	other
P-value	= 1
Method	Fisher exact
Parameter estimate	Percent reduction
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	98.7

Secondary: Number of subjects with severe gastroenteritis (GE)

End point title	Number of subjects with severe gastroenteritis (GE)

End point description:

Severe GE was defined as a GE episode requiring hospitalization and/or re-hydration therapy in a medical facility.

End point type	Secondary

End point timeframe:

During the study period for the long-term follow-up (i.e. 6 months)

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1065	525		
Units: Subjects	15	6		

Statistical analyses

Statistical analysis title	Vaccine efficacy with respect to severe GE

Statistical analysis description:

Vaccine efficacy with respect to severe gastroenteritis (GE).Vaccine efficacy (VE) was defined as the percent reduction in the frequency of the relevant outcome variable in vaccinated subjects compared with those subjects who received placebo.

Comparison groups	Rotarix Group v Placebo Group
Number of subjects included in analysis	1590
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.817
Method	Fisher exact
Parameter estimate	Percent reduction
Point estimate	-23.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-287.7
upper limit	54.8

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

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

End point description:

An SAE was any untoward medical occurrence that resulted in death, was life-threatening, required hospitalization or prolongation of existing hospitalization, resulted in disability/incapacity or was a congenital anomaly/birth defect in the offspring of a study subject.

End point type	Secondary

End point timeframe:

During the study period for the long-term follow-up (i.e. 6 months)

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1082	531		
Units: Subjects	4	7		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting intussusception (IS)

End point title	Number of subjects reporting intussusception (IS)

End point description:

Intussusception is defined as the telescoping of the intestine.

End point type	Secondary

End point timeframe:

During the period starting from the end of the second follow-up period up to the start of the study (up to 6 months)

End point values	Rotarix Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1082	531		
Units: Subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Serious adverse events (SAEs): during the study period for the long-term follow-up (i.e. 6 months)

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	11.0

Reporting groups

Reporting group title	Rotarix Group

Reporting group description:

Healthy children between and including 6 to 12 weeks of age at the time of first vaccination, who received two powdered oral doses of Rotarix vaccine in the Rota-036 primary vaccination study (102247), were subsequently followed-up for 6 months during their third year of age, in scope of the present study.

Reporting group title	Placebo Group

Reporting group description:

Healthy children between and including 6 to 12 weeks of age at the time of first vaccination, who received two liquid oral doses of placebo in the Rota-036 primary vaccination study (102247), were subsequently followed-up for 6 months during their third year of age, in scope of the present study.

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: The were no non-serious adverse events recorded for this study.

Serious adverse events	Rotarix Group	Placebo Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 1082 (0.37%)	7 / 531 (1.32%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Nervous system disorders			
Febrile convulsion			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 1082 (0.00%)	1 / 531 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Asthma			
alternative assessment type: Non-systematic			

subjects affected / exposed	1 / 1082 (0.09%)	1 / 531 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Gastroenteritis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 1082 (0.09%)	1 / 531 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 1082 (0.00%)	2 / 531 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 1082 (0.09%)	0 / 531 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 1082 (0.00%)	1 / 531 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 1082 (0.09%)	0 / 531 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 1082 (0.00%)	1 / 531 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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	0 / 1082 (0.00%)	0 / 531 (0.00%)	

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