



## Clinical trial results:

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

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

## Summary

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

## Results information

Result version number	v2
This version publication date	07 May 2016
First version publication date	08 July 2015
Version creation reason	• Correction of full data set Data correction due to a system error in EudraCT – Results

## Trial information

### Trial identification

Sponsor protocol code	109216
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### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00432380
WHO universal trial number (UTN)	-

Notes:

## Sponsors

Sponsor organisation name	GlaxoSmithKline Biologicals
Sponsor organisation address	Rue de l'Institut 89, Rixensart, Belgium, B-1330
Public contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com
Scientific contact	Clinical Trials Call Center, GlaxoSmithKline Biologicals, 044 2089-904466, GSKClinicalSupportHD@gsk.com

Notes:

## Paediatric regulatory details

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

Notes:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	04 September 2007
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 September 2007
Global end of trial reached?	Yes
Global end of trial date	04 September 2007
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

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

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

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

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Philippines: 375
Worldwide total number of subjects	375
EEA total number of subjects	0

Notes:

### Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	375
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0
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## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

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

### Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	PL-V-V Group

Arm description:

Subjects received GlaxoSmithKline (GSK) Biologicals' oral live attenuated human rotavirus vaccine (HRV) liquid vaccine at Month 1 and Month 2 and placebo at Day 0.

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

Dosage and administration details:

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

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

Dosage and administration details:

1 oral dose of placebo administered at Day 0.

<b>Arm title</b>	V-PL-V Group
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Arm description:

Subjects received HRV liquid vaccine at Day 0 and Month 2 and placebo at Month 1.

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

Dosage and administration details:

Two oral doses of the liquid HRV vaccine administered at Day 0 and Month 2.

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

Dosage and administration details:

1 oral dose of placebo administered at Month 1.

<b>Arm title</b>	Placebo Group
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Arm description:

Subjects received placebo at Day 0, Month 1 and Month 2.

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

Dosage and administration details:

Three oral doses of placebo administered at Day 0, Months 1 and 2.

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

## Baseline characteristics

### Reporting groups

Reporting group title	PL-V-V Group
Reporting group description:	
Subjects received GlaxoSmithKline (GSK) Biologicals' oral live attenuated human rotavirus vaccine (HRV) liquid vaccine at Month 1 and Month 2 and placebo at Day 0.	
Reporting group title	V-PL-V Group
Reporting group description:	
Subjects received HRV liquid vaccine at Day 0 and Month 2 and placebo at Month 1.	
Reporting group title	Placebo Group
Reporting group description:	
Subjects received placebo at Day 0, Month 1 and Month 2.	

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

Reporting group values	Total		
Number of subjects	375		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	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			
standard deviation	-		
Gender categorical			
Units: Subjects			
Female	175		
Male	200		

## End points

### End points reporting groups

Reporting group title	PL-V-V Group
Reporting group description: Subjects received GlaxoSmithKline (GSK) Biologicals' oral live attenuated human rotavirus vaccine (HRV) liquid vaccine at Month 1 and Month 2 and placebo at Day 0.	
Reporting group title	V-PL-V Group
Reporting group description: Subjects received HRV liquid vaccine at Day 0 and Month 2 and placebo at Month 1.	
Reporting group title	Placebo Group
Reporting group description: Subjects received placebo at Day 0, Month 1 and Month 2.	

### Primary: Number of seroconverted subjects for Anti-RV IgA antibody in PL-V-V Group.

End point title	Number of seroconverted subjects for Anti-RV IgA antibody in PL-V-V Group. <sup>[1][2]</sup>
End point description: Seroconversion was defined as the appearance of anti-rotavirus IgA antibody concentration $\geq 20$ units (U)/ millilitre (ml) in subjects initially (i.e. prior to the first dose of HRV vaccine or placebo) seronegative. This outcome measure concerns subjects in the PL-V-V Group only.	
End point type	Primary
End point timeframe: At Month 3 (i.e. Visit 4) when administered concomitantly with the second and third routine EPI immunization.	
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. [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: This outcome measure concerns subjects in the PL-V-V Group only.	

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

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of seroconverted subjects for Anti-RV IgA antibody in V-PL-V Group.

End point title	Number of seroconverted subjects for Anti-RV IgA antibody in V-PL-V Group. <sup>[3]</sup>
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End point description:

Seroconversion was defined as the appearance of anti-rotavirus IgA antibody concentration  $\geq 20$  units (U)/ millilitre (ml) in subjects initially (i.e. prior to the first dose of HRV vaccine or placebo) seronegative. This outcome measure concerns subjects in the V-PL-V Group only.

End point type	Secondary
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End point timeframe:

At Month 3 (i.e. Visit 4) when administered concomitantly with the first and third routine EPI immunization.

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This outcome measure concerns subjects in the V-PL-V Group only.

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

## Statistical analyses

No statistical analyses for this end point

## Secondary: Serum IgA antibody titres against rotavirus.

End point title	Serum IgA antibody titres against rotavirus. <sup>[4]</sup>
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End point description:

Antibody titres were summarized by geometric mean concentrations (GMCs) with their 95% CIs. None of the subjects in the placebo group were seroconverted. This outcome measure concerns subjects in PL-V-V and V-PL-V Groups.

End point type	Secondary
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End point timeframe:

At Month 3 (i.e. Visit 4).

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: This outcome measure concerns subjects in PL-V-V and V-PL-V Groups.

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

## Statistical analyses

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

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

Any symptom = occurrence of the symptom (i.e. fever or vomiting or diarrhea) regardless of intensity grade or relationship to vaccination.

Grade 2 fever = Rectal temperature greater than ( $>$ ) 38.5 – less than or equal to ( $\leq$ ) 39.5°C or axillary temperature  $> 38.0 - \leq 39.0^{\circ}\text{C}$ , Grade 3 fever = Rectal temperature  $> 39.5^{\circ}\text{C}$  or axillary temperature  $> 39.0^{\circ}\text{C}$ , Grade 2 vomiting = 2 episodes of vomiting/ day, Grade 3 vomiting = greater than or equal to ( $\geq$ ) 3 episodes of vomiting/ day, Grade 2 diarrhea = 4-5 looser than normal stools/ day and Grade 3 diarrhea =  $\geq 6$  looser than normal stools/ day.

End point type	Secondary
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## End point timeframe:

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

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

**Statistical analyses**

No statistical analyses for this end point

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

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

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

End point type	Secondary
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End point timeframe:

During the 8-day (Day 0-Day 7) solicited follow-up period after each dose of HRV liquid vaccine or placebo and overall.

<b>End point values</b>	PL-V-V Group	V-PL-V Group	Placebo Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	150	150	75	
Units: Subjects				
Any Cough/ runny nose, Dose 1 [N=150, 150, 75]	52	44	23	
Grade 3 Cough/ runny nose, Dose 1 [N=150, 150, 75]	0	1	1	
Related Cough/ runny nose, Dose 1 [N=150, 150, 75]	1	0	1	
Any Diarrhea, Dose 1 [N=150, 150, 75]	5	4	6	
Grade 3 Diarrhea, Dose 1 [N=150, 150, 75]	2	0	0	
Related Diarrhea, Dose 1 [N=150, 150, 75]	5	4	5	
Any Fever, Dose 1 [N=150, 150, 75]	122	117	54	
Grade 3 Fever, Dose 1 [N=150, 150, 75]	3	5	0	
Related Fever, Dose 1 [N=150, 150, 75]	121	114	53	
Any Irritability, Dose 1 [N=150, 150, 75]	87	72	34	
Grade 3 Irritability, Dose 1 [N=150, 150, 75]	3	5	0	
Related Irritability, Dose 1 [N=150, 150, 75]	81	70	34	
Any Loss of appetite, Dose 1 [N=150, 150, 75]	26	35	17	
Grade 3 Loss of appetite, Dose 1 [N=150, 150, 75]	1	0	0	
Related Loss of appetite, Dose 1 [N=150, 150, 75]	20	31	15	
Any Vomiting, Dose 1 [N=150, 150, 75]	32	24	5	
Grade 3 Vomiting, Dose 1 [N=150, 150, 75]	2	1	2	
Related Vomiting, Dose 1 [N=150, 150, 75]	23	21	5	
Any Cough/ runny nose, Dose 2 [N=149, 147, 75]	48	37	21	
Grade 3 Cough/ runny nose, Dose 2 [N=149, 147, 75]	2	0	1	
Related Cough/ runny nose, Dose 2 [N=149, 147, 75]	0	0	1	
Any Diarrhea, Dose 2 [N=149, 147, 75]	3	1	0	
Grade 3 Diarrhea, Dose 2 [N=149, 147, 75]	1	0	0	
Related Diarrhea, Dose 2 [N=149, 147, 75]	1	1	0	
Any Fever, Dose 2 [N=149, 147, 75]	103	94	45	
Grade 3 Fever, Dose 2 [N=149, 147, 75]	3	4	2	

Related Fever, Dose 2 [N=149, 147, 75]	102	93	45	
Any Irritability, Dose 2 [N=149, 147, 75]	55	45	24	
Grade 3 Irritability, Dose 2 [N=149, 147, 75]	0	0	0	
Related Irritability, Dose 2 [N=149, 147, 75]	52	43	24	
Any Loss of appetite, Dose 2 [N=149, 147, 75]	20	21	8	
Grade 3 Loss of appetite, Dose 2 [N=149, 147, 75]	0	0	1	
Related Loss of appetite, Dose 2 [N=149, 147, 75]	16	20	7	
Any Vomiting, Dose 2 [N=149, 147, 75]	15	17	5	
Grade 3 Vomiting, Dose 2 [N=149, 147, 75]	0	1	0	
Related Vomiting, Dose 2 [N=149, 147, 75]	11	14	4	
Any Cough/ runny nose, Dose 3 [N= 146, 147, 75]	36	31	23	
Grade 3 Cough/ runny nose, Dose 3 [N= 146, 147, 75]	0	6	1	
Related Cough/ runny nose, Dose 3 [N= 146, 147, 75]	0	0	0	
Any Diarrhea, Dose 3 [N= 146, 147, 75]	2	1	1	
Grade 3 Diarrhea, Dose 3 [N= 146, 147, 75]	0	0	0	
Related Diarrhea, Dose 3 [N= 146, 147, 75]	2	1	1	
Any Fever, Dose 3 [N= 146, 147, 75]	91	91	48	
Grade 3 Fever, Dose 3 [N= 146, 147, 75]	3	5	2	
Related Fever, Dose 3 [N= 146, 147, 75]	87	89	47	
Any Irritability, Dose 3 [N= 146, 147, 75]	33	40	21	
Grade 3 Irritability, Dose 3 [N= 146, 147, 75]	0	3	2	
Related Irritability, Dose 3 [N= 146, 147, 75]	31	38	20	
Any Loss of appetite, Dose 3 [N= 146, 147, 75]	19	18	7	
Grade 3 Loss of appetite, Dose 3 [N= 146, 147, 75]	0	1	0	
Related Loss of appetite, Dose 3 [N= 146, 147, 75]	19	17	7	
Any Vomiting, Dose 3 [N= 146, 147, 75]	10	8	1	
Grade 3 Vomiting, Dose 3 [N= 146, 147, 75]	0	2	0	
Related Vomiting, Dose 3 [N= 146, 147, 75]	8	4	1	
Any Cough/runny nose, Across doses [N=150, 150, 75]	82	69	40	
Grade 3 Cough/runny nose, Across doses [N=150, 150, 75]	2	6	2	
Related Cough/runny nose, Across doses [N=150, 150, 75]	1	0	2	
Any Diarrhea, Across doses [N= 150, 150, 75]	8	6	7	

Grade 3 Diarrhea, Across doses [N= 150, 150, 75]	3	0	0	
Related Diarrhea, Across doses [N= 150, 150, 75]	6	6	6	
Any Temperature, Across doses [N= 150, 150, 75]	139	137	69	
Grade 3 Temperature, Across doses [N= 150, 150, 75]	8	13	3	
Related Temperature, Across doses [N= 150, 150, 75]	138	135	69	
Any Irritability, Across doses [N= 150, 150, 75]	93	78	40	
Grade 3 Irritability, Across doses [N= 150, 150, 75]	3	7	2	
Related Irritability, Across doses [N= 150, 150, 75]	90	76	40	
Any Loss of appetite, Across doses [N=150,150,75]	40	46	23	
Grade 3 Loss of appetite, Across doses [N=150,150,75]	1	1	1	
Related Loss of appetite, Across doses [N=150,150,75]	35	42	21	
Any Vomiting, Across doses [N= 150, 150, 75]	35	32	9	
Grade 3 Vomiting, Across doses [N= 150, 150, 75]	2	3	2	
Related Vomiting, Across doses [N= 150, 150, 75]	27	26	8	

## Statistical analyses

No statistical analyses for this end point

## Secondary: Presence of rotavirus (RV) in gastroenteritis (GE) stools.

End point title	Presence of rotavirus (RV) in gastroenteritis (GE) stools.
End point description:	
Number of subjects reporting RV (vaccine strain or wild-type) GE episode(s).	
End point type	Secondary
End point timeframe:	
From Dose 1 of HRV vaccine or placebo up to visit 4 (i.e. Month 3).	

End point values	PL-V-V Group	V-PL-V Group	Placebo Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	150	150	75	
Units: Subjects				
Between Dose 1 and before Dose 2 [N=150, 150, 75]	1	0	1	
Between Dose 2 and before Dose 3 [N=149, 147, 75]	0	0	0	
Between Dose 3 and Visit 4 [N= 146, 147, 75]	0	0	0	

Between Dose 1 and Visit 4 [N= 150, 150, 75]	1	0	1	
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## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subjects reporting any unsolicited adverse event.

End point title	Number of subjects reporting any unsolicited adverse event.
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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
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End point timeframe:

During the 31-day (Day 0-Day 30) follow-up period after any doses of HRV liquid vaccine or placebo.

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

## Statistical analyses

No statistical analyses for this end point

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

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

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

End point type	Secondary
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End point timeframe:

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

<b>End point values</b>	PL-V-V Group	V-PL-V Group	Placebo Group	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	150	150	75	
Units: Subjects				
Any SAE(s)	1	1	1	

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms were collected during the 8-day (Days 0-7) post vaccination period. Unsolicited AEs were collected during the 31 day (Days 0-30) post vaccination. SAEs were collected throughout the entire study period (Months 0 to 3).

Adverse event reporting additional description:

The number of occurrences reported for solicited symptoms, adverse events, and serious adverse events were not available for posting. The number of subjects affected by each specific event was indicated as the number of occurrences.

Assessment type	Non-systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	10.1
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### Reporting groups

Reporting group title	PL-V-V Group
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Reporting group description:

Subjects received GlaxoSmithKline (GSK) Biologicals' oral live attenuated human rotavirus vaccine (HRV) liquid vaccine at Month 1 and Month 2 and placebo at Day 0.

Reporting group title	Placebo Group
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Reporting group description:

Subjects received placebo at Day 0, Month 1 and Month 2.

Reporting group title	V-PL-V Group
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Reporting group description:

Subjects received HRV liquid vaccine at Day 0 and Month 2 and placebo at Month 1.

Serious adverse events	PL-V-V Group	Placebo Group	V-PL-V Group
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 150 (0.67%)	1 / 75 (1.33%)	1 / 150 (0.67%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Immune system disorders			
Milk allergy			
subjects affected / exposed	0 / 150 (0.00%)	0 / 75 (0.00%)	1 / 150 (0.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis salmonella			
subjects affected / exposed	1 / 150 (0.67%)	0 / 75 (0.00%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			



subjects affected / exposed	0 / 150 (0.00%)	1 / 75 (1.33%)	0 / 150 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

<b>Non-serious adverse events</b>	PL-V-V Group	Placebo Group	V-PL-V Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	139 / 150 (92.67%)	69 / 75 (92.00%)	137 / 150 (91.33%)
General disorders and administration site conditions			
Cough/runny nose, Dose 1			
alternative assessment type: Systematic			
subjects affected / exposed	52 / 150 (34.67%)	23 / 75 (30.67%)	44 / 150 (29.33%)
occurrences (all)	52	23	44
Diarrhea, Dose 1			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 150 (3.33%)	6 / 75 (8.00%)	4 / 150 (2.67%)
occurrences (all)	5	6	4
Fever (Rectally), Dose 1			
alternative assessment type: Systematic			
subjects affected / exposed	122 / 150 (81.33%)	54 / 75 (72.00%)	117 / 150 (78.00%)
occurrences (all)	122	54	117
Irritability, Dose 1			
alternative assessment type: Systematic			
subjects affected / exposed	87 / 150 (58.00%)	34 / 75 (45.33%)	72 / 150 (48.00%)
occurrences (all)	87	34	72
Loss of appetite, Dose 1			
alternative assessment type: Systematic			
subjects affected / exposed	26 / 150 (17.33%)	17 / 75 (22.67%)	35 / 150 (23.33%)
occurrences (all)	26	17	35
Vomiting, Dose 1			
alternative assessment type: Systematic			
subjects affected / exposed	32 / 150 (21.33%)	5 / 75 (6.67%)	24 / 150 (16.00%)
occurrences (all)	32	5	24

Cough/runny nose, Dose 2 alternative assessment type: Systematic subjects affected / exposed <sup>[1]</sup> occurrences (all)	48 / 149 (32.21%) 48	21 / 75 (28.00%) 21	37 / 147 (25.17%) 37
Fever (Rectally), Dose 2 alternative assessment type: Systematic subjects affected / exposed <sup>[2]</sup> occurrences (all)	103 / 149 (69.13%) 103	45 / 75 (60.00%) 45	94 / 147 (63.95%) 94
Irritability, Dose 2 alternative assessment type: Systematic subjects affected / exposed <sup>[3]</sup> occurrences (all)	55 / 149 (36.91%) 55	24 / 75 (32.00%) 24	45 / 147 (30.61%) 45
Loss of appetite, Dose 2 alternative assessment type: Systematic subjects affected / exposed <sup>[4]</sup> occurrences (all)	20 / 149 (13.42%) 20	8 / 75 (10.67%) 8	21 / 147 (14.29%) 21
Vomiting, Dose 2 alternative assessment type: Systematic subjects affected / exposed <sup>[5]</sup> occurrences (all)	15 / 149 (10.07%) 15	5 / 75 (6.67%) 5	17 / 147 (11.56%) 17
Cough/runny nose, Dose 3 alternative assessment type: Systematic subjects affected / exposed <sup>[6]</sup> occurrences (all)	36 / 146 (24.66%) 36	23 / 75 (30.67%) 23	31 / 147 (21.09%) 31
Fever (Rectally), Dose 3 alternative assessment type: Systematic subjects affected / exposed occurrences (all)	91 / 150 (60.67%) 91	48 / 75 (64.00%) 48	91 / 150 (60.67%) 91
Irritability, Dose 3 alternative assessment type: Systematic subjects affected / exposed <sup>[7]</sup> occurrences (all)	33 / 146 (22.60%) 33	21 / 75 (28.00%) 21	40 / 147 (27.21%) 40
Loss of appetite, Dose 3 alternative assessment type: Systematic			

subjects affected / exposed <sup>[8]</sup>	19 / 146 (13.01%)	7 / 75 (9.33%)	18 / 147 (12.24%)
occurrences (all)	19	7	18
Vomiting, Dose 3			
alternative assessment type: Systematic			
subjects affected / exposed <sup>[9]</sup>	10 / 146 (6.85%)	1 / 75 (1.33%)	8 / 147 (5.44%)
occurrences (all)	10	1	8
Cough/runny nose, Across doses			
alternative assessment type: Systematic			
subjects affected / exposed	82 / 150 (54.67%)	40 / 75 (53.33%)	69 / 150 (46.00%)
occurrences (all)	82	40	69
Diarrhea, Across doses			
alternative assessment type: Systematic			
subjects affected / exposed	8 / 150 (5.33%)	7 / 75 (9.33%)	6 / 150 (4.00%)
occurrences (all)	8	7	6
Fever (Rectally), Across doses			
alternative assessment type: Systematic			
subjects affected / exposed	139 / 150 (92.67%)	69 / 75 (92.00%)	137 / 150 (91.33%)
occurrences (all)	139	69	137
Irritability, Across doses			
alternative assessment type: Systematic			
subjects affected / exposed	93 / 150 (62.00%)	40 / 75 (53.33%)	78 / 150 (52.00%)
occurrences (all)	93	40	78
Loss of appetite, Across doses			
alternative assessment type: Systematic			
subjects affected / exposed	40 / 150 (26.67%)	23 / 75 (30.67%)	46 / 150 (30.67%)
occurrences (all)	40	23	46
Vomiting, Across doses			
alternative assessment type: Systematic			
subjects affected / exposed	35 / 150 (23.33%)	9 / 75 (12.00%)	32 / 150 (21.33%)
occurrences (all)	35	9	32
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	19 / 150 (12.67%)	6 / 75 (8.00%)	21 / 150 (14.00%)
occurrences (all)	19	6	21
Rhinitis			

subjects affected / exposed	13 / 150 (8.67%)	6 / 75 (8.00%)	16 / 150 (10.67%)
occurrences (all)	13	6	16
Bronchitis			
subjects affected / exposed	7 / 150 (4.67%)	4 / 75 (5.33%)	7 / 150 (4.67%)
occurrences (all)	7	4	7
Diarrhea infectious			
subjects affected / exposed	5 / 150 (3.33%)	2 / 75 (2.67%)	9 / 150 (6.00%)
occurrences (all)	5	2	9

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)

[7] - 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)

[8] - 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)

[9] - 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? Yes

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

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported