Clinical trial results:
A phase III, double-blind, randomised, placebo-controlled, multi-country and multi-center study to assess the efficacy, immunogenicity and safety of two doses of GSK Biologicals' oral live attenuated human rotavirus (HRV) vaccine given concomitantly with routine expanded program on immunisation (EPI) vaccinations including oral poliovirus vaccine (OPV) in healthy infants.

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

Summary

EudraCT number	2015-001540-10
Trial protocol	Outside EU/EEA
Global end of trial date	20 March 2007

Results information

Result version number	v2 (current)
This version publication date	07 May 2016
First version publication date	28 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	444563/024

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00139347
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	12 October 2007
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 March 2007
Global end of trial reached?	Yes
Global end of trial date	20 March 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine if two doses of GSK Biologicals' HRV vaccine given concomitantly with routine EPI vaccinations including OPV can prevent severe rotavirus gastroenteritis (RV GE) caused by the circulating wild-type RV strains during the period starting from 2 weeks after Dose 2 until one year of age.

Protection of trial subjects:

Subjects 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	03 December 2003
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	Honduras: 450
Country: Number of subjects enrolled	Brazil: 485
Country: Number of subjects enrolled	Dominican Republic: 450
Country: Number of subjects enrolled	Colombia: 1674
Country: Number of subjects enrolled	Argentina: 2618
Country: Number of subjects enrolled	Panama: 891
Worldwide total number of subjects	6568
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)	6568
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

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

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	HRV Group

Arm description:

Subjects received 2 doses of GlaxoSmithKline (GSK) Biologicals' human rotavirus (HRV) vaccine according to a 0, 1 to 2-month schedule with the routine EPI vaccinations.

Arm type	Experimental
Investigational medicinal product name	Rotarix
Investigational medicinal product code	
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 HRV vaccine administered to healthy infants who are 6-12 weeks of age.

Arm title	Placebo Group

Arm description:

Subjects received 2 doses of placebo according to a 0, 1 to 2-month schedule with the routine EPI vaccinations.

Arm type	Experimental
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:

Two oral doses of plavebo administered to healthy infants who are 6-12 weeks of age.

Number of subjects in period 1	HRV Group	Placebo Group
Started	4376	2192
Completed	4234	2115
Not completed	142	77
Adverse event, serious fatal	11	3
Consent withdrawn by subject	60	33
Adverse event, non-fatal	1	-
Migrated/moved from study area	48	24
Unspecified	3	-
Lost to follow-up	18	16
Protocol deviation	1	1

Baseline characteristics

Reporting groups	
Reporting group title	HRV Group
Reporting group description:	
Subjects received 2 doses of GlaxoSmithKline (GSK) Biologicals' human rotavirus (HRV) vaccine according to a 0, 1 to 2-month schedule with the routine EPI vaccinations.	
Reporting group title	Placebo Group
Reporting group description:	
Subjects received 2 doses of placebo according to a 0, 1 to 2-month schedule with the routine EPI vaccinations.	

Reporting group values	HRV Group	Placebo Group	Total
Number of subjects	4376	2192	6568
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	8.6	8.6	
standard deviation	± 1.3	± 1.33	-
Gender categorical			
Units: Subjects			
Female	2198	1090	3288
Male	2178	1102	3280

End points

End points reporting groups

Reporting group title	HRV Group
Reporting group description:	
Subjects received 2 doses of GlaxoSmithKline (GSK) Biologicals' human rotavirus (HRV) vaccine according to a 0, 1 to 2-month schedule with the routine EPI vaccinations.	
Reporting group title	Placebo Group
Reporting group description:	
Subjects received 2 doses of placebo according to a 0, 1 to 2-month schedule with the routine EPI vaccinations.	

Primary: Number of subjects with severe rotavirus gastroenteritis (RV GE) caused by the wild-type RV strain

End point title	Number of subjects with severe rotavirus gastroenteritis (RV GE) caused by the wild-type RV strain[1]
End point description:	
Severe RV GE episodes were defined as an episode of severe gastroenteritis occurring at least two weeks after the full vaccination course in which rotavirus other than vaccine strain was identified in a stool sample collected as soon as possible but not later than 7 days after admission to the hospital or medical facility	
End point type	Primary
End point timeframe:	
From 2 weeks after Dose 2 up to study end	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The analysis of the primary endpoint was descriptive i.e. no statistical hypothesis test was performed.

End point values	HRV Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4211	2099		
Units: Subjects				
RV GE episodes	7	19		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with severe RV GE caused by the wild RV strain of serotype G1

End point title	Number of subjects with severe RV GE caused by the wild RV strain of serotype G1
End point description:	
Severe GE episode was defined as a gastroenteritis episode requiring hospitalization and/or re-hydration therapy (equivalent to WHO plan B or C) in a medical facility.	
End point type	Secondary

End point timeframe:

From 2 weeks after Dose 2 until one year of age

End point values	HRV Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4211	2099		
Units: Subjects				
G1 wild type +P8 wild type	0	1		
G2+P4	1	2		
G9+P8 wild type	6	16		
Pooled Non G1 (G2, G9)	7	18		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with severe RV GE due to non-G1 serotypes

End point title	Number of subjects with severe RV GE due to non-G1 serotypes

End point description:

Severe GE episode was defined as a gastroenteritis episode requiring hospitalization and/or re-hydration therapy (equivalent to WHO plan B or C) in a medical facility.

End point type	Secondary

End point timeframe:

From 2 weeks after Dose 2 until one year of age

End point values	HRV Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4376	2192		
Units: Subjects				
Severe RV GE	8	23		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with severe RV GE episode, by isolated RV types

End point title	Number of subjects with severe RV GE episode, by isolated RV types

End point description:

Severe GE episode was defined as a gastroenteritis episode requiring hospitalization and/or re-hydration therapy (equivalent to WHO plan B or C) in a medical facility.

End point type	Secondary

End point timeframe:

From Dose 1 up to study end

End point values	HRV Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4376	2192		
Units: Subjects				
G1 wild type +P8 wild type	0	1		
G2+P4	1	3		
G9+P8 wild type	7	19		
Pooled Non G1 (G2, G9)	8	22		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Serious adverse event was defined as any untoward medical occurrence that resulted in death, was life-threatening, required hospitalization or prolongation of existing hospitalization, resulted in disability/incapacity, was a congenital anomaly/birth defect in the offspring of a study subject, an important medical events that may not be immediately life-threatening or resulted in death or hospitalization but may have jeopardized the subject or required medical or surgical intervention to prevent one of the other outcomes.

End point type	Secondary

End point timeframe:

Throughout the study period (Month 0 to Month 10)

End point values	HRV Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4376	2192		
Units: Subjects				
Any SAE(s)	505	265		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum rotavirus immunoglobulin A (IgA) antibody concentrations

End point title	Serum rotavirus immunoglobulin A (IgA) antibody

	concentrations

End point description:

Antibody concentrations were summarized by Geometric Mean Concentrations (GMCs) with their 95% CIs. This analysis was performed on a subset of 300 subjects enrolled in year 2003-2004.

End point type	Secondary

End point timeframe:

At one to two months after the second study vaccine dose (at Visit 3)

End point values	HRV Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	89	176		
Units: U/mL				
geometric mean (confidence interval 95%)				
Anti- IgA	18 (13.1 to 24.6)	66 (49.9 to 87.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Serum rotavirus immunoglobulin A (IgA) antibody concentrations

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

End point description:

Antibody titers were summarized by Geometric Mean Titers (GMTs) with their 95% CIs. This analysis was performed on a subset of 300 subjects enrolled in year 2003-2004.

End point type	Secondary

End point timeframe:

At one to two months after the second dose of routine EPI vaccinations (at Visit 3)

End point values	HRV Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	168	83		
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-polio 1 (N= 168, 80)	710.6 (549.9 to 918.3)	1064.8 (803.2 to 1411.6)		
Anti-polio 2 (N= 165, 83)	819.6 (651.7 to 1030.8)	1326.5 (1020.4 to 1724.5)		
Anti-polio 3 (N= 164, 81)	117.5 (89 to 155)	162.7 (109.7 to 241.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroprotected for anti-polio type 1, type 2 and type 3 antibodies

End point title	Number of subjects seroprotected for anti-polio type 1, type 2 and type 3 antibodies

End point description:

A seroprotected subject was defined as a subject with antibody concentration/titer greater than or equal to the seroprotection level. This analysis was performed on a subset of 300 subjects enrolled in year 2003-2004.

End point type	Secondary

End point timeframe:

At one to two months after the second dose of routine EPI vaccinations (at Visit 3)

End point values	HRV Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	168	83		
Units: Subjects				
Anti-polio 1 (N= 168, 80)	163	80		
Anti-polio 2 (N= 165, 83)	160	82		
Anti-polio 3 (N= 164, 81)	138	70		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations for anti- polyribosyl ribitol phosphate (PRP) antibodies

End point title	Antibody concentrations for anti- polyribosyl ribitol phosphate (PRP) antibodies

End point description:

Antibody concentrations were summarized by Geometric Mean Concentrations (GMCs) with their 95% CIs. This analysis was performed on a subset of 300 subjects enrolled in year 2003-2004.

End point type	Secondary

End point timeframe:

At one to two months after the third dose of routine EPI vaccinations (at Visit 4)

End point values	HRV Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	179	91		
Units: µg/mL				
geometric mean (confidence interval 95%)				
Anti-PRP	20.426 (17.183 to 24.281)	18.99 (14.134 to 25.514)		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations for anti-diphtheria (anti-D) and anti-tetanus (anti-T) antibodies.

End point title	Antibody concentrations for anti-diphtheria (anti-D) and anti-tetanus (anti-T) antibodies.

End point description:

Antibody concentrations were summarized by Geometric Mean Concentrations (GMCs) with their 95% CIs. This analysis was performed on a subset of 300 subjects enrolled in year 2003-2004.

End point type	Secondary

End point timeframe:

At one to two months after the third dose of routine EPI vaccinations (at Visit 4)

End point values	HRV Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	181	90		
Units: IU/mL				
geometric mean (confidence interval 95%)				
Anti-D	0.656 (0.534 to 0.805)	0.696 (0.52 to 0.932)		
Anti-T	2.988 (2.582 to 3.459)	2.669 (2.16 to 3.297)		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations for anti-Bordetella pertussis toxoids (anti-BPT) antibodies.

End point title	Antibody concentrations for anti-Bordetella pertussis toxoids (anti-BPT) antibodies.

End point description:

Antibody concentrations were summarized by Geometric Mean Concentrations (GMCs) with their 95% CIs. This analysis was performed on a subset of 300 subjects enrolled in year 2003-2004.

End point type	Secondary

End point timeframe:

At one to two months after the third dose of routine EPI vaccinations (at Visit 4)

End point values	HRV Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	181	90		
Units: EL.U/mL				
geometric mean (confidence interval 95%)				
Anti-BPT	68.2 (60 to 77.6)	58.6 (48.3 to 71.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody concentrations for anti-hepatitis B surface antigen (anti-HBs) antibodies.

End point title	Antibody concentrations for anti-hepatitis B surface antigen (anti-HBs) antibodies.

End point description:

Antibody concentrations were summarized by Geometric Mean Concentrations (GMCs) with their 95% CIs. This analysis was performed on a subset of 300 subjects enrolled in year 2003-2004.

End point type	Secondary

End point timeframe:

At one to two months after the third dose of routine EPI vaccinations (at Visit 4)

End point values	HRV Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	176	90		
Units: mIU/mL				
geometric mean (confidence interval 95%)				
Anti-HBs	1007.8 (813.2 to 1248.9)	899.6 (659.1 to 1227.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody titers against poliovirus type 1, 2 and 3.

End point title	Antibody titers against poliovirus type 1, 2 and 3.

End point description:

Antibody titers were summarized by Geometric Mean Titers (GMTs) with their 95% CIs. This analysis was performed on a subset of 300 subjects enrolled in year 2003-2004.

End point type	Secondary

End point timeframe:

At one to two months after the third dose of routine EPI vaccinations (at Visit 4)

End point values	HRV Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	177	90		
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-polio 1 (N= 173, 86)	989.5 (796.9 to 1228.7)	967.8 (742.9 to 1261)		
Anti-polio 2 (N= 174, 90)	792 (665.7 to 942.2)	898.2 (724.8 to 1113.2)		
Anti-polio 3 (N= 177, 90)	156.3 (127.1 to 192.3)	154 (122.7 to 193.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seropositive for anti-BPT antibodies

End point title	Number of subjects seropositive for anti-BPT antibodies

End point description:

A seropositive subject was defined as a subject whose titer was greater than or equal to the cut-off value (≥ 15 EL. U/mL). This analysis was performed on a subset of 300 subjects enrolled in year 2003-2004.

End point type	Secondary

End point timeframe:

At one to two months after the third dose of routine EPI vaccinations (at Visit 4)

End point values	HRV Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	181	90		
Units: Subjects				
Anti-BPT ≥ 15 EL.U/mL	171	83		

Statistical analyses

No statistical analyses for this end point

Secondary: Antibody titers against poliovirus type 1, 2 and 3.

End point title	Antibody titers against poliovirus type 1, 2 and 3.

End point description:

Antibody titers were summarized by Geometric Mean Titers (GMTs) with their 95% CIs. This analysis was performed on a subset of 900 subjects enrolled in year 2005.

End point type	Secondary

End point timeframe:

At one month after each dose of routine EPI vaccinations (at Month 1, Month 3 and Month 5)

End point values	HRV Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	522	251		
Units: Titers				
geometric mean (confidence interval 95%)				
Anti-polio 1; M1 (N= 487, 243)	221.3 (184.6 to 265.2)	313.3 (243.4 to 403.2)		
Anti-polio 1; M3 (N= 506, 242)	908.8 (782.2 to 1055.8)	1417.4 (1193.3 to 1683.6)		
Anti-polio 1; M5 (N= 491, 236)	1259.3 (1109.7 to 1429.1)	1495.8 (1282.2 to 1745)		
Anti-polio 2; M1 (N= 458, 224)	289.6 (251.7 to 333.3)	257.1 (208 to 317.8)		
Anti-polio 2; M3 (N= 494, 228)	1290.8 (1149.4 to 1449.6)	1472.4 (1263.4 to 1715.9)		
Anti-polio 2; M5 (N= 494, 243)	1246.3 (1122.5 to 1383.8)	1216.9 (1064.3 to 1391.4)		
Anti-polio 3; M1 (N= 522, 251)	17.6 (14.8 to 20.9)	20.4 (16 to 26)		
Anti-polio 3; M3 (N= 499, 234)	132.4 (113.1 to 154.9)	172.6 (139.2 to 214.1)		
Anti-polio 3; M5 (N= 513, 251)	232.2 (207.6 to 259.8)	267.7 (229.1 to 312.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects seroprotected for anti-polio type 1, type 2 and type 3 antibodies

End point title	Number of subjects seroprotected for anti-polio type 1, type 2 and type 3 antibodies

End point description:

A seroprotected subject was defined as a subject with antibody concentration/titer greater than or equal to the seroprotection level. This analysis was performed on a subset of 900 subjects enrolled in year 2005.

End point type	Secondary

End point timeframe:

At one month after each dose of routine EPI vaccinations (at Month 1, Month 3 and Month 5)

End point values	HRV Group	Placebo Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	522	251		
Units: Subjects				
Anti-polio 1; M1 (N= 487, 243)	445	230		
Anti-polio 1; M3 (N= 506, 242)	491	240		
Anti-polio 1; M5 (N= 491, 236)	487	236		
Anti-polio 2; M1 (N= 458, 224)	445	214		
Anti-polio 2; M3 (N= 494, 228)	491	228		
Anti-polio 2; M5 (N= 494, 243)	494	243		
Anti-polio 3; M1 (N= 522, 251)	222	120		
Anti-polio 3; M3 (N= 499, 234)	434	213		
Anti-polio 3; M5 (N= 513, 251)	504	248		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

The occurrence of reported AEs (all/related) was not available and is 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	HRV Group

Reporting group description:

Subjects received 2 doses of GlaxoSmithKline (GSK) Biologicals' human rotavirus (HRV) vaccine according to a 0, 1 to 2-month schedule with the routine EPI vaccinations.

Reporting group title	Placebo Group

Reporting group description:

Subjects received 2 doses of placebo according to a 0, 1 to 2-month schedule with the routine EPI vaccinations.

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: No non-serious adverse events were reported.

Serious adverse events	HRV Group	Placebo Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	505 / 4376 (11.54%)	265 / 2192 (12.09%)	
number of deaths (all causes)	10	2	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neuroblastoma			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypovolaemic shock			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Pyrexia			

subjects affected / exposed	6 / 4376 (0.14%)	3 / 2192 (0.14%)	
occurrences causally related to treatment / all	1 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypothermia			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multi-organ failure			
subjects affected / exposed	0 / 4376 (0.00%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 4376 (0.00%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Social circumstances			
Child abuse			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Bronchial obstruction			
subjects affected / exposed	25 / 4376 (0.57%)	13 / 2192 (0.59%)	
occurrences causally related to treatment / all	0 / 25	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	10 / 4376 (0.23%)	6 / 2192 (0.27%)	
occurrences causally related to treatment / all	0 / 10	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial hyper reactivity			
subjects affected / exposed	3 / 4376 (0.07%)	3 / 2192 (0.14%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

Bronchospasm			
subjects affected / exposed	2 / 4376 (0.05%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Apnea			
subjects affected / exposed	2 / 4376 (0.05%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	2 / 4376 (0.05%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	1 / 4376 (0.02%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthmatic crisis			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foreign body aspiration			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleurisy			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleurocutaneous fistula			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory disorder			

subjects affected / exposed	0 / 4376 (0.00%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	15 / 4376 (0.34%)	6 / 2192 (0.27%)	
occurrences causally related to treatment / all	0 / 15	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thermal burn			
subjects affected / exposed	2 / 4376 (0.05%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 4376 (0.00%)	2 / 2192 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skull fracture			
subjects affected / exposed	1 / 4376 (0.02%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic brain injury			
subjects affected / exposed	1 / 4376 (0.02%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Accidental exposure			
subjects affected / exposed	0 / 4376 (0.00%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Accidental poisoning			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amoebic dysentery			

subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaesthetic complication			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Burns second degree			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug toxicity			
subjects affected / exposed	0 / 4376 (0.00%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye injury			
subjects affected / exposed	0 / 4376 (0.00%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple injuries			
subjects affected / exposed	0 / 4376 (0.00%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Poisoning			

subjects affected / exposed	0 / 4376 (0.00%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Sickle cell anemia			
subjects affected / exposed	2 / 4376 (0.05%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital syphilis			
subjects affected / exposed	0 / 4376 (0.00%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Aortic valve stenosis			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac arrest			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cyanosis			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Convulsion			
subjects affected / exposed	4 / 4376 (0.09%)	9 / 2192 (0.41%)	
occurrences causally related to treatment / all	0 / 4	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	

Febrile convulsion			
subjects affected / exposed	7 / 4376 (0.16%)	4 / 2192 (0.18%)	
occurrences causally related to treatment / all	0 / 7	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	2 / 4376 (0.05%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infantile spasms			
subjects affected / exposed	0 / 4376 (0.00%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial pressure increased			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Partial seizures			
subjects affected / exposed	0 / 4376 (0.00%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post-traumatic epilepsy			
subjects affected / exposed	0 / 4376 (0.00%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	2 / 4376 (0.05%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemolysis			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Idiopathic thrombocytopenic purpura			

subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency anemia			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenitis			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	6 / 4376 (0.14%)	4 / 2192 (0.18%)	
occurrences causally related to treatment / all	0 / 6	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intussusception			
subjects affected / exposed	4 / 4376 (0.09%)	2 / 2192 (0.09%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Diarrhea			
subjects affected / exposed	3 / 4376 (0.07%)	2 / 2192 (0.09%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastro esophageal reflux disease			
subjects affected / exposed	3 / 4376 (0.07%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			

subjects affected / exposed	2 / 4376 (0.05%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal hemorrhage			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematemesis			
subjects affected / exposed	0 / 4376 (0.00%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis atopic			
subjects affected / exposed	0 / 4376 (0.00%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			

subjects affected / exposed	0 / 4376 (0.00%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bronchiolitis			
subjects affected / exposed	148 / 4376 (3.38%)	64 / 2192 (2.92%)	
occurrences causally related to treatment / all	0 / 148	0 / 64	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastroenteritis			
subjects affected / exposed	95 / 4376 (2.17%)	65 / 2192 (2.97%)	
occurrences causally related to treatment / all	1 / 95	0 / 65	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	91 / 4376 (2.08%)	47 / 2192 (2.14%)	
occurrences causally related to treatment / all	0 / 91	0 / 47	
deaths causally related to treatment / all	0 / 2	0 / 0	
Bronchopneumonia			
subjects affected / exposed	41 / 4376 (0.94%)	22 / 2192 (1.00%)	
occurrences causally related to treatment / all	0 / 41	0 / 22	
deaths causally related to treatment / all	0 / 1	0 / 0	
Urinary tract infection			
subjects affected / exposed	20 / 4376 (0.46%)	10 / 2192 (0.46%)	
occurrences causally related to treatment / all	0 / 20	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	13 / 4376 (0.30%)	8 / 2192 (0.36%)	
occurrences causally related to treatment / all	0 / 13	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	

Bronchitis			
subjects affected / exposed	15 / 4376 (0.34%)	5 / 2192 (0.23%)	
occurrences causally related to treatment / all	0 / 15	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	8 / 4376 (0.18%)	3 / 2192 (0.14%)	
occurrences causally related to treatment / all	0 / 8	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			
subjects affected / exposed	7 / 4376 (0.16%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 7	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			
subjects affected / exposed	5 / 4376 (0.11%)	2 / 2192 (0.09%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	5 / 4376 (0.11%)	2 / 2192 (0.09%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media acute			
subjects affected / exposed	2 / 4376 (0.05%)	5 / 2192 (0.23%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Croup infectious			
subjects affected / exposed	2 / 4376 (0.05%)	3 / 2192 (0.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngotracheo bronchitis			
subjects affected / exposed	3 / 4376 (0.07%)	2 / 2192 (0.09%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pertussis			

subjects affected / exposed	3 / 4376 (0.07%)	2 / 2192 (0.09%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	4 / 4376 (0.09%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Abscess			
subjects affected / exposed	2 / 4376 (0.05%)	2 / 2192 (0.09%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	4 / 4376 (0.09%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis rotavirus			
subjects affected / exposed	2 / 4376 (0.05%)	2 / 2192 (0.09%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasopharyngitis			
subjects affected / exposed	3 / 4376 (0.07%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis bacterial			
subjects affected / exposed	0 / 4376 (0.00%)	3 / 2192 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis bacterial			
subjects affected / exposed	2 / 4376 (0.05%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Otitis media			

subjects affected / exposed	3 / 4376 (0.07%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngotonsillitis			
subjects affected / exposed	1 / 4376 (0.02%)	2 / 2192 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	2 / 4376 (0.05%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteremia			
subjects affected / exposed	2 / 4376 (0.05%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Exanthema subitum			
subjects affected / exposed	2 / 4376 (0.05%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impetigo			
subjects affected / exposed	2 / 4376 (0.05%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngitis			
subjects affected / exposed	1 / 4376 (0.02%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngotracheitis			
subjects affected / exposed	1 / 4376 (0.02%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis tuberculous			

subjects affected / exposed	1 / 4376 (0.02%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis viral			
subjects affected / exposed	2 / 4376 (0.05%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	2 / 4376 (0.05%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 4376 (0.02%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Rhinitis			
subjects affected / exposed	1 / 4376 (0.02%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess limb			
subjects affected / exposed	0 / 4376 (0.00%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acarodermatitis			
subjects affected / exposed	0 / 4376 (0.00%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacterial infection			

subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bullous impetigo			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Conjunctivitis bacterial			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dengue fever			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Empyema			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis bacterial			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Enteritis			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpangina			
subjects affected / exposed	0 / 4376 (0.00%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			

subjects affected / exposed	0 / 4376 (0.00%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lobar pneumonia			
subjects affected / exposed	0 / 4376 (0.00%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung abscess			
subjects affected / exposed	0 / 4376 (0.00%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis			
subjects affected / exposed	0 / 4376 (0.00%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis aseptic			
subjects affected / exposed	0 / 4376 (0.00%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parasitic infection intestinal			
subjects affected / exposed	0 / 4376 (0.00%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perianal abscess			
subjects affected / exposed	0 / 4376 (0.00%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			

subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary tuberculosis			
subjects affected / exposed	0 / 4376 (0.00%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	0 / 4376 (0.00%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scarlet fever			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Skin bacterial infection			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal sepsis			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	0 / 4376 (0.00%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			

subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheitis			
subjects affected / exposed	0 / 4376 (0.00%)	1 / 2192 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicella			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral diarrhea			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral rash			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	7 / 4376 (0.16%)	7 / 2192 (0.32%)	
occurrences causally related to treatment / all	0 / 7	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malnutrition			
subjects affected / exposed	3 / 4376 (0.07%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lactose intolerance			

subjects affected / exposed	2 / 4376 (0.05%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	1 / 4376 (0.02%)	0 / 2192 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	HRV Group	Placebo Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 4376 (0.00%)	0 / 2192 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 May 2004	• The procedures for the surveillance of the hospital and/or medical facilities in the involved study areas were re-aligned across countries to take into consideration of the operating reality of the different study settings. Complementary surveillance procedures were expected to improve timely identification of severe GE cases. • The active hospital surveillance for severe GE case collection were complemented by subject surveillance, when needed. • In the same context the interval window for stool collection was widened to 7 days after admission to a medical facility or hospital. • The safety data obtained in studies with GSK Biologicals' HRV vaccine were updated.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported