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

Summary

EudraCT number	2015-001485-26
Trial protocol	Outside EU/EEA
Global end of trial date	30 January 2009

Results information

Result version number	v1 (current)
This version publication date	20 April 2016
First version publication date	23 July 2015

Trial information

Trial identification

Sponsor protocol code	102248,111274

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00241644
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	15 June 2009
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 January 2009
Global end of trial reached?	Yes
Global end of trial date	30 January 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine if the GSK Biologicals' HRV vaccine (pooled HRV groups) given concomitantly with routine EPI vaccinations can prevent severe RV GE (>11 on the 20-point Vesikari scoring system) caused by the circulating wild-type RV strains during the period from 2 weeks after the last dose of HRV vaccine or placebo until Visit 6.
Criteria: The primary objective will be reached if the lower limit of the 95% CI on vaccine efficacy is > 0%.

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	24 October 2005
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	South Africa: 3168
Country: Number of subjects enrolled	Malawi: 1773
Worldwide total number of subjects	4941
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)	4941
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:

Only subjects from Malawi and from Cohort 2 South Africa were asked to continue the study for a second follow-up period (Year 2).

Pre-assignment

Screening details:

Of the total of 4941 subjects enrolled in this study, 2 subjects were allocated a subject number but did not get any study vaccine administered. Hence, only 4939 subjects were considered as 'started'. For the second follow-up period, as mentioned in the protocol the results are presented for Rotarix Pooled and Placebo Groups only.

Period 1

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

Blinding implementation details:

The study was conducted in a double-blind manner with respect to GSK Biologicals' oral live attenuated human rotavirus (HRV) vaccine and placebo. The parents/guardians of the subjects, the study personnel and the investigator were unaware of the administered treatment (HRV vaccine or placebo).

Arms

Are arms mutually exclusive?	Yes
Arm title	Rotarix 2-dose Group

Arm description:

Subjects received 1 dose of placebo followed by 2 doses of Rotarix™ vaccine given concomitantly with routine EPI vaccines.

Arm type	Experimental
Investigational medicinal product name	Rotarix™
Investigational medicinal product code	
Other name	GSK Biologicals’ HRV vaccine
Pharmaceutical forms	Powder and solvent for oral suspension
Routes of administration	Oral use

Dosage and administration details:

Two or Three doses, oral administration.

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:

One or three doses, oral administration.

Arm title	Rotarix 3-dose Group

Arm description:

Subjects received 3 doses of Rotarix™ vaccine given concomitantly with routine EPI vaccines.

Arm type	Experimental

Investigational medicinal product name	Rotarix™
Investigational medicinal product code	
Other name	GSK Biologicals' HRV vaccine
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Two or Three doses, oral administration.

Arm title	Placebo Group

Arm description:

Subjects received 3 doses of placebo given concomitantly with routine EPI vaccines.

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

Dosage and administration details:

One or three doses, oral administration.

Number of subjects in period 1[1]	Rotarix 2-dose Group	Rotarix 3-dose Group	Placebo Group
Started	1647	1651	1641
Completed; Visit 6	1420	1383	1392
Completed	1420	1383	1392
Not completed	227	268	249
Return dates not reliable	1	-	-
Consent withdrawn by subject	59	74	81
Adverse event, non-fatal	46	45	45
Non-compliance	2	1	2
Subject's parent passed away	-	1	-
Lost to follow-up	116	142	116
Vaccinated at regular clinic	-	-	1
Protocol deviation	3	5	4

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: withOf the total of 4941 subjects enrolled in this study, 2 subjects were allocated a subject number but did not get any study vaccine administered. Hence, only 4939 subjects were considered as 'started'.

Period 2

Period 2 title	Second efficacy period (Year 2)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Rotarix 2-dose Group

Arm description:

Subjects received 1 dose of placebo followed by 2 doses of Rotarix™ vaccine given concomitantly with routine EPI vaccines.

Arm type	Experimental
Investigational medicinal product name	Rotarix™
Investigational medicinal product code	
Other name	GSK Biologicals' HRV vaccine
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Two or Three doses, oral administration.

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

Dosage and administration details:

One or three doses, oral administration.

Arm title	Rotarix 3-dose Group

Arm description:

Subjects received 3 doses of Rotarix™ vaccine given concomitantly with routine EPI vaccines.

Arm type	Experimental
Investigational medicinal product name	Rotarix™
Investigational medicinal product code	
Other name	GSK Biologicals' HRV vaccine
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Two or Three doses, oral administration.

Arm title	Placebo Group

Arm description:

Subjects received 3 doses of placebo given concomitantly with routine EPI vaccines.

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

Dosage and administration details:

One or three doses, oral administration.

Number of subjects in period 2[2]	Rotarix 2-dose Group	Rotarix 3-dose Group	Placebo Group
Started	771	754	746
Completed	710	697	682
Not completed	61	57	64
Consent withdrawn by subject	4	3	2
Adverse event, non-fatal	11	9	12
Consenting parent passed away	1	1	2
Lost to follow-up	43	43	46
Protocol deviation	2	1	2

Notes:

[2] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: For the second follow-up period, as mentioned in the protocol the results are presented for Rotarix Pooled and Placebo Groups only.

Baseline characteristics

Reporting groups	
Reporting group title	Rotarix 2-dose Group
Reporting group description:	
Subjects received 1 dose of placebo followed by 2 doses of Rotarix™ vaccine given concomitantly with routine EPI vaccines.	
Reporting group title	Rotarix 3-dose Group
Reporting group description:	
Subjects received 3 doses of Rotarix™ vaccine given concomitantly with routine EPI vaccines.	
Reporting group title	Placebo Group
Reporting group description:	
Subjects received 3 doses of placebo given concomitantly with routine EPI vaccines.	

Reporting group values	Rotarix 2-dose Group	Rotarix 3-dose Group	Placebo Group
Number of subjects	1647	1651	1641
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	6.3	6.4	6.4
standard deviation	± 0.92	± 0.98	± 0.97
Gender categorical Units: Subjects			
Female	811	839	800
Male	836	812	841

Reporting group values	Total		
Number of subjects	4939		
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	2450		
Male	2489		

Subject analysis sets

Subject analysis set title	Rotarix Pooled Group (Year 1)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

For some data analyses, the 2 Groups receiving Rotarix (Rotarix 2-dose Group & Rotarix 3-dose Group) were pooled into Rotarix pooled Group.

Subject analysis set title	Rotarix Pooled Group (Year 2)
Subject analysis set type	Sub-group analysis

Subject analysis set description:

For some data analyses, the 2 Groups receiving Rotarix (Rotarix 2-dose Group & Rotarix 3-dose Group) were pooled into Rotarix pooled Group.

Reporting group values	Rotarix Pooled Group (Year 1)	Rotarix Pooled Group (Year 2)	
Number of subjects	3298	1525	
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	6.4		
standard deviation	± 0.95	±	
Gender categorical			
Units: Subjects			
Female	1650		
Male	1648		

End points

End points reporting groups

Reporting group title	Rotarix 2-dose Group
Reporting group description:	
Subjects received 1 dose of placebo followed by 2 doses of Rotarix™ vaccine given concomitantly with routine EPI vaccines.	
Reporting group title	Rotarix 3-dose Group
Reporting group description:	
Subjects received 3 doses of Rotarix™ vaccine given concomitantly with routine EPI vaccines.	
Reporting group title	Placebo Group
Reporting group description:	
Subjects received 3 doses of placebo given concomitantly with routine EPI vaccines.	
Reporting group title	Rotarix 2-dose Group
Reporting group description:	
Subjects received 1 dose of placebo followed by 2 doses of Rotarix™ vaccine given concomitantly with routine EPI vaccines.	
Reporting group title	Rotarix 3-dose Group
Reporting group description:	
Subjects received 3 doses of Rotarix™ vaccine given concomitantly with routine EPI vaccines.	
Reporting group title	Placebo Group
Reporting group description:	
Subjects received 3 doses of placebo given concomitantly with routine EPI vaccines.	
Subject analysis set title	Rotarix Pooled Group (Year 1)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
For some data analyses, the 2 Groups receiving Rotarix (Rotarix 2-dose Group & Rotarix 3-dose Group) were pooled into Rotarix pooled Group.	
Subject analysis set title	Rotarix Pooled Group (Year 2)
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
For some data analyses, the 2 Groups receiving Rotarix (Rotarix 2-dose Group & Rotarix 3-dose Group) were pooled into Rotarix pooled Group.	

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

End point title	Number of subjects with severe rotavirus gastroenteritis (RV GE) caused by the circulating wild-type rotavirus strain.[1]
End point description:	
Number of subjects presenting with three or more looser than normal stools or watery stools within a day, occurring after administration of dose 1 of study vaccine in which rotavirus other than vaccine strain was identified in a stool sample with a score ≥ 11 on the 20-point Vesikari scoring system. This outcome measure concerns subjects in the Rotarix 2-dose Group	
End point type	Primary
End point timeframe:	
From 2 weeks after the last vaccine or placebo dose up to 1 year of age.	

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	Rotarix 2-dose Group	Rotarix 3-dose Group	Placebo Group	Rotarix Pooled Group (Year 1)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	1496	1478	1443	2974
Units: Subjects	30	26	70	56

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with severe rotavirus gastroenteritis caused by the circulating wild-type rotavirus strain, classified by rotavirus type.

End point title	Number of subjects with severe rotavirus gastroenteritis caused by the circulating wild-type rotavirus strain, classified by rotavirus type.

End point description:

Number of subjects presenting with three or more looser than normal stools within a day, occurring after administration of dose 1 of study vaccine in which rotavirus other than vaccine strain was identified in a stool sample with a score ≥ 11 on the 20-point Vesikari scoring system. Rotavirus types were G1 wild type (WT) and non-G1.

End point type	Secondary

End point timeframe:

From 2 weeks after the last vaccine or placebo dose up to 1 year of age.

End point values	Rotarix 2-dose Group	Rotarix 3-dose Group	Placebo Group	Rotarix Pooled Group (Year 1)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	1496	1478	1443	2974
Units: Subjects				
G1 WT	8	9	23	17
Non-G1	22	17	47	39

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any rotavirus gastroenteritis caused by the circulating wild-type rotavirus strain.

End point title	Number of subjects reporting any rotavirus gastroenteritis caused by the circulating wild-type rotavirus strain.

End point description:

Number of subjects presenting with three or more looser than normal stools or watery stools within a day, occurring after administration of dose 1 of study vaccine in which rotavirus other than vaccine strain was identified in a stool sample.

End point type	Secondary

End point timeframe:

From 2 weeks after the last vaccine or placebo dose up to 1 year of age.

End point values	Rotarix 2-dose Group	Rotarix 3-dose Group	Placebo Group	Rotarix Pooled Group (Year 1)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	1496	1478	1443	2974
Units: Subjects	93	74	174	167

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with severe rotavirus gastroenteritis caused by the circulating wild-type rotavirus strain.

End point title	Number of subjects with severe rotavirus gastroenteritis caused by the circulating wild-type rotavirus strain.

End point description:

Number of subjects presenting with three or more looser than normal stools or watery stools within a day, occurring after administration of dose 1 of study vaccine in which rotavirus other than vaccine strain was identified in a stool sample with a score ≥ 11 on the 20-point Vesikari scoring system.

End point type	Secondary

End point timeframe:

From the first vaccine or placebo dose up to 1 year of age.

End point values	Rotarix 2-dose Group	Rotarix 3-dose Group	Placebo Group	Rotarix Pooled Group (Year 1)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	1647	1651	1641	3298
Units: Subjects	37	31	83	68

Statistical analyses

No statistical analyses for this end point

Secondary: In South Africa, number of subjects with severe rotavirus gastroenteritis caused by the circulating wild-type rotavirus strain.

End point title	In South Africa, number of subjects with severe rotavirus gastroenteritis caused by the circulating wild-type rotavirus strain.

End point description:

Number of subjects presenting with three or more looser than normal stools or watery stools within a day, occurring after administration of dose 1 of study vaccine in which rotavirus other than vaccine strain was identified in a stool sample with a score ≥ 11 on the 20-point Vesikari scoring system.

End point type	Secondary

End point timeframe:

From 2 weeks after the third dose of vaccine or placebo up to 1 year of age.

End point values	Rotarix 2-dose Group	Rotarix 3-dose Group	Placebo Group	Rotarix Pooled Group (Year 2)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	478	468	468	946
Units: Subjects	5	3	20	8

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting severe gastroenteritis of any cause.

End point title	Number of subjects reporting severe gastroenteritis of any cause.

End point description:

Number of subjects with gastroenteritis (three or more looser than normal stools or watery stools within a day) that scored ≥ 11 on the 20-point Vesikari scoring system.

End point type	Secondary

End point timeframe:

From 2 weeks after the last vaccine or placebo dose up to 1 year of age.

End point values	Rotarix 2-dose Group	Rotarix 3-dose Group	Placebo Group	Rotarix Pooled Group (Year 1)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	1496	1478	1443	2974
Units: Subjects	134	122	178	256

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects hospitalized and/or with supervised re-hydration therapy due to rotavirus gastroenteritis (RV GE) caused by the circulating wild-type rotavirus strain.

End point title	Number of subjects hospitalized and/or with supervised re-hydration therapy due to rotavirus gastroenteritis (RV GE) caused by the circulating wild-type rotavirus strain.

End point description:

RV GE caused by the circulating wild-type rotavirus strain: three or more looser than normal stools or watery stools within a day, occurring after administration of dose 1 of study vaccine in which rotavirus other than vaccine strain was identified in a stool sample collected as soon as possible after the symptoms begin.

End point type	Secondary

End point timeframe:

From 2 weeks after the last vaccine or placebo dose up to 1 year of age.

End point values	Rotarix 2-dose Group	Rotarix 3-dose Group	Placebo Group	Rotarix Pooled Group (Year 1)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	1496	1478	1443	2974
Units: Subjects	78	64	156	142

Statistical analyses

No statistical analyses for this end point

Secondary: For subjects in Cohort 2 South Africa and the cohort in Malawi: Number of subjects with severe rotavirus gastroenteritis (RV GE) caused by the circulating wild-type rotavirus strains.

End point title	For subjects in Cohort 2 South Africa and the cohort in Malawi: Number of subjects with severe rotavirus gastroenteritis (RV GE) caused by the circulating wild-type rotavirus strains.[2]

End point description:

Number of subjects presenting with three or more looser than normal stools or watery stools within a day, occurring after administration of dose 1 of study vaccine in which rotavirus other than vaccine strain was identified in a stool sample with a score ≥ 11 on the 20-point Vesikari scoring system. This outcome measure concerns subjects in the Placebo group from the first efficacy period and the Rotarix pooled group (Year 1) only.

End point type	Secondary

End point timeframe:

During the period from 2 weeks after the last dose of vaccine or placebo until study end.

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: This outcome measure concerns subjects in the Placebo group from the first efficacy period and the Rotarix pooled group (Year 1) only.

End point values	Placebo Group	Rotarix Pooled Group (Year 1)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	891	1873		
Units: Subjects	81	66		

Statistical analyses

No statistical analyses for this end point

Secondary: For subjects in Cohort 2 South Africa and the cohort in Malawi: Number of subjects with severe rotavirus gastroenteritis (RV GE) caused by the circulating wild-type rotavirus strains.

End point title	For subjects in Cohort 2 South Africa and the cohort in Malawi: Number of subjects with severe rotavirus gastroenteritis (RV GE) caused by the circulating wild-type rotavirus strains.

End point description:

Number of subjects presenting with three or more looser than normal stools or watery stools within a day, occurring after administration of dose 1 of study vaccine in which rotavirus other than vaccine strain was identified in a stool sample with a score ≥ 11 on the 20-point Vesikari scoring system.

End point type	Secondary

End point timeframe:

During the period from 1 year of age to study end.

End point values	Placebo Group	Rotarix Pooled Group (Year 2)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	712	1500		
Units: Subjects	21	35		

Statistical analyses

No statistical analyses for this end point

Secondary: For subjects in Cohort 2 South Africa and the cohort in Malawi: Number of subjects hospitalized and/or with supervised re-hydration therapy due to rotavirus gastroenteritis (RV GE) episode caused by the circulating wild-type RV strains.

End point title	For subjects in Cohort 2 South Africa and the cohort in Malawi: Number of subjects hospitalized and/or with supervised re-hydration therapy due to rotavirus gastroenteritis (RV GE) episode caused by the circulating wild-type RV strains.[3]

End point description:

RV GE caused by the circulating wild-type rotavirus strain: three or more looser than normal stools or watery stools within a day, occurring after administration of dose 1 of study vaccine in which rotavirus other than vaccine strain was identified in a stool sample collected as soon as possible after the symptoms begin. This outcome measure concerns subjects in the Placebo group from the first efficacy period and the Rotarix pooled group (Year 1) only.

End point type	Secondary

End point timeframe:

During the period from 2 weeks after the last dose of vaccine or placebo until study end.

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 Placebo group from the first efficacy period and the Rotarix pooled group (Year 1) only.

End point values	Placebo Group	Rotarix Pooled Group (Year 1)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	891	1873		
Units: Subjects	118	159		

Statistical analyses

No statistical analyses for this end point

Secondary: For subjects in Cohort 2 South Africa and the cohort in Malawi: Number of subjects hospitalized and/or with supervised re-hydration therapy due to rotavirus gastroenteritis (RV GE) episode caused by the circulating wild-type RV strains.

End point title	For subjects in Cohort 2 South Africa and the cohort in Malawi: Number of subjects hospitalized and/or with supervised re-hydration therapy due to rotavirus gastroenteritis (RV GE) episode caused by the circulating wild-type RV strains.

End point description:

RV GE caused by the circulating wild-type rotavirus strain: three or more looser than normal stools or watery stools within a day, occurring after administration of dose 1 of study vaccine in which rotavirus other than vaccine strain was identified in a stool sample collected as soon as possible after the symptoms begin.

End point type	Secondary

End point timeframe:

During the period from 1 year of age to study end.

End point values	Placebo Group	Rotarix Pooled Group (Year 2)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	712	1500		
Units: Subjects	26	58		

Statistical analyses

No statistical analyses for this end point

Secondary: For subjects in Cohort 2 South Africa and the cohort in Malawi: Number of subjects with severe rotavirus gastroenteritis caused by the circulating wild-type rotavirus strains, classified by rotavirus type.

End point title	For subjects in Cohort 2 South Africa and the cohort in Malawi: Number of subjects with severe rotavirus gastroenteritis caused by the circulating wild-type rotavirus strains, classified by rotavirus type.[4]

End point description:

Number of subjects presenting with three or more looser than normal stools or watery stools within a day, occurring after administration of dose 1 of study vaccine in which rotavirus other than vaccine strain was identified in a stool sample with a score ≥ 11 on the 20-point Vesikari scoring system. Rotavirus types were G1 wild type (WT) and non-G1. This outcome measure concerns subjects in the Placebo group from the first efficacy period and the Rotarix pooled group (Year 1) only.

End point type	Secondary

End point timeframe:

During the period from 2 weeks after the last dose of vaccine or placebo until study end.

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 the Placebo group from the first efficacy period and the Rotarix pooled group (Year 1) only.

End point values	Placebo Group	Rotarix Pooled Group (Year 1)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	891	1873		
Units: Subjects				
G1 WT	20	21		
Non-G1	48	60		

Statistical analyses

No statistical analyses for this end point

Secondary: For subjects in Cohort 2 South Africa and the cohort in Malawi: Number of subjects with severe rotavirus gastroenteritis caused by the circulating wild-type rotavirus strains, classified by rotavirus type.

End point title	For subjects in Cohort 2 South Africa and the cohort in Malawi: Number of subjects with severe rotavirus gastroenteritis caused by the circulating wild-type rotavirus strains, classified by rotavirus type.

End point description:

Number of subjects presenting with three or more looser than normal stools or watery stools within a day, occurring after administration of dose 1 of study vaccine in which rotavirus other than vaccine strain was identified in a stool sample with a score ≥ 11 on the 20-point Vesikari scoring system. Rotavirus types were G1 wild type (WT) and non-G1.

End point type	Secondary

End point timeframe:

During the period from 1 year of age to study end.

End point values	Placebo Group	Rotarix Pooled Group (Year 2)		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	712	1500		
Units: Subjects				
G1 WT	11	10		
Non-G1	10	25		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with adverse events (AEs) or serious adverse events (SAEs) leading to drop out.

End point title	Number of subjects with adverse events (AEs) or serious adverse events (SAEs) leading to drop out.

End point description:

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

End point type	Secondary

End point timeframe:

From the first dose of vaccine or placebo up to end of the study.

End point values	Rotarix 2-dose Group	Rotarix 3-dose Group	Placebo Group	Rotarix Pooled Group (Year 1)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	1647	1651	1641	3298
Units: Subjects				
Any AEs/SAEs	57	54	56	111

Statistical analyses

No statistical analyses for this end point

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

End point type	Secondary

End point timeframe:

From the first dose of vaccine or placebo up to end of the study.

End point values	Rotarix 2-dose Group	Rotarix 3-dose Group	Placebo Group	Rotarix Pooled Group (Year 1)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	1647	1651	1641	3298
Units: Subjects				
Any SAE(s)	222	199	246	421

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric mean concentration of anti-rotavirus immunoglobulin A (IgA) antibodies in initially seronegative subjects.

End point title	Geometric mean concentration of anti-rotavirus immunoglobulin A (IgA) antibodies in initially seronegative subjects.

End point description:

An initially seronegative subject is a subject whose IgA antibody concentration was below the assay cut-off value of 20 Units per milliliter (U/mL) before administration of the first vaccine dose.

End point type	Secondary

End point timeframe:

One month after the last vaccine dose.

End point values	Rotarix 2-dose Group	Rotarix 3-dose Group	Placebo Group	Rotarix Pooled Group (Year 2)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	106	115	111	221
Units: U/mL				
geometric mean (confidence interval 95%)	56.6 (38.9 to 82.3)	79.4 (54.7 to 115.2)	67.5 (51.9 to 87.8)	23.4 (16.8 to 32.5)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted subjects.

End point title	Number of seroconverted subjects.

End point description:

Seroconverted subjects are defined as subjects with appearance of anti-rotavirus IgA antibody concentration ≥ 20 U/mL in subjects initially (i.e. prior to the first dose of vaccine or placebo) seronegative for rotavirus.

End point type	Secondary

End point timeframe:

One month after the last vaccine or placebo dose.

End point values	Rotarix 2-dose Group	Rotarix 3-dose Group	Placebo Group	Rotarix Pooled Group (Year 2)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	106	115	111	221
Units: Subjects	57	72	25	129

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric mean concentration of anti-rotavirus immunoglobulin A (IgA) antibodies.

End point title	Geometric mean concentration of anti-rotavirus immunoglobulin A (IgA) antibodies.

End point description:

Geometric mean concentrations are given as Units per milliliter (U/mL).

End point type	Secondary

End point timeframe:

One month after the last vaccine or placebo dose.

End point values	Rotarix 2-dose Group	Rotarix 3-dose Group	Placebo Group	Rotarix Pooled Group (Year 1)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	1160	1138	1125	2298
Units: U/mL				
geometric mean (confidence interval 95%)	72.5 (65.2 to 80.6)	67.9 (60.8 to 75.9)	21.8 (19.8 to 24)	70.2 (65 to 75.8)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects.

End point title	Number of seropositive subjects.

End point description:

Seropositive subjects are defined as subjects with anti-rotavirus IgA antibody concentration ≥ 20 U/mL.

End point type	Secondary

End point timeframe:

One month after the last vaccine or placebo dose.

End point values	Rotarix 2-dose Group	Rotarix 3-dose Group	Placebo Group	Rotarix Pooled Group (Year 1)
Subject group type	Reporting group	Reporting group	Reporting group	Subject analysis set
Number of subjects analysed	1160	1138	1125	2298
Units: Subjects	756	706	262	1462

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 entire study period.

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

Dictionary used

Dictionary name	MedDRA
Dictionary version	11.0

Reporting groups

Reporting group title	Rotarix 2-dose Group

Reporting group description:

Subjects received 1 dose of placebo followed by 2 doses of Rotarix™ (rotavirus vaccine).

Reporting group title	Rotarix 3-dose Group

Reporting group description:

Subjects received 3 doses of Rotarix™ (rotavirus vaccine).

Reporting group title	Rotarix pooled Group

Reporting group description:

For some data analyses, the 2 Groups receiving Rotarix (Rotarix 2-dose Group & Rotarix 3-dose Group) were pooled into Rotarix pooled Group.

Reporting group title	Placebo Group

Reporting group description:

Subjects received 3 doses of placebo.

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 adverse events (non-serious) with frequency equal to or greater than 5% were reported.

Serious adverse events	Rotarix 2-dose Group	Rotarix 3-dose Group	Rotarix pooled Group
Total subjects affected by serious adverse events			
subjects affected / exposed	222 / 1647 (13.48%)	199 / 1651 (12.05%)	421 / 3298 (12.77%)
number of deaths (all causes)	2	2	4
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neuroblastoma			
subjects affected / exposed	1 / 1647 (0.06%)	0 / 1651 (0.00%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Adenoidectomy			

subjects affected / exposed	1 / 1647 (0.06%)	0 / 1651 (0.00%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Death			
subjects affected / exposed	2 / 1647 (0.12%)	2 / 1651 (0.12%)	4 / 3298 (0.12%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 4
deaths causally related to treatment / all	0 / 2	0 / 2	0 / 4
Pyrexia			
subjects affected / exposed	1 / 1647 (0.06%)	3 / 1651 (0.18%)	4 / 3298 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden infant death syndrome			
subjects affected / exposed	0 / 1647 (0.00%)	2 / 1651 (0.12%)	2 / 3298 (0.06%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 2
Cyst			
subjects affected / exposed	0 / 1647 (0.00%)	1 / 1651 (0.06%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Irritability			
subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Immunosuppression			
subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Reproductive system and breast disorders			
Genital rash			
subjects affected / exposed	1 / 1647 (0.06%)	0 / 1651 (0.00%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	3 / 1647 (0.18%)	2 / 1651 (0.12%)	5 / 3298 (0.15%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	3 / 1647 (0.18%)	0 / 1651 (0.00%)	3 / 3298 (0.09%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 3	0 / 0	0 / 3
Asphyxia			
subjects affected / exposed	0 / 1647 (0.00%)	2 / 1651 (0.12%)	2 / 3298 (0.06%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 2
Aspiration			
subjects affected / exposed	0 / 1647 (0.00%)	1 / 1651 (0.06%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Bronchospasm			
subjects affected / exposed	0 / 1647 (0.00%)	1 / 1651 (0.06%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	1 / 1647 (0.06%)	0 / 1651 (0.00%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory arrest			

subjects affected / exposed	0 / 1647 (0.00%)	1 / 1651 (0.06%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Respiratory failure			
subjects affected / exposed	0 / 1647 (0.00%)	1 / 1651 (0.06%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Atelectasis			
subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnea			
subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Grunting			
subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenoidal hypertrophy			
subjects affected / exposed	0 / 1647 (0.00%)	1 / 1651 (0.06%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foreign body aspiration			

subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Thermal burn			
subjects affected / exposed	2 / 1647 (0.12%)	4 / 1651 (0.24%)	6 / 3298 (0.18%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Brachial plexus injury			
subjects affected / exposed	1 / 1647 (0.06%)	0 / 1651 (0.00%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fractured skull depressed			
subjects affected / exposed	1 / 1647 (0.06%)	0 / 1651 (0.00%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
subjects affected / exposed	2 / 1647 (0.12%)	0 / 1651 (0.00%)	2 / 3298 (0.06%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury			
subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis chemical			
subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue injury			

subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Therapeutic agent toxicity			
subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chemical poisoning			
subjects affected / exposed	1 / 1647 (0.06%)	0 / 1651 (0.00%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin laceration			
subjects affected / exposed	0 / 1647 (0.00%)	1 / 1651 (0.06%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug toxicity			
subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Heart disease congenital			
subjects affected / exposed	1 / 1647 (0.06%)	1 / 1651 (0.06%)	2 / 3298 (0.06%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Patent ductus arteriosus			
subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Phimosis			
subjects affected / exposed	0 / 1647 (0.00%)	1 / 1651 (0.06%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			

Cardiac failure congestive			
subjects affected / exposed	0 / 1647 (0.00%)	1 / 1651 (0.06%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemic shock			
subjects affected / exposed	0 / 1647 (0.00%)	1 / 1651 (0.06%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Tachycardia			
subjects affected / exposed	1 / 1647 (0.06%)	0 / 1651 (0.00%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	4 / 1647 (0.24%)	7 / 1651 (0.42%)	11 / 3298 (0.33%)
occurrences causally related to treatment / all	0 / 4	0 / 7	0 / 11
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalitis			
subjects affected / exposed	1 / 1647 (0.06%)	0 / 1651 (0.00%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Status epilepticus			
subjects affected / exposed	1 / 1647 (0.06%)	1 / 1651 (0.06%)	2 / 3298 (0.06%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 2
Convulsion			
subjects affected / exposed	1 / 1647 (0.06%)	2 / 1651 (0.12%)	3 / 3298 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Fontanelle bulging			
subjects affected / exposed	0 / 1647 (0.00%)	1 / 1651 (0.06%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrocephalus			

subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	2 / 1647 (0.12%)	6 / 1651 (0.36%)	8 / 3298 (0.24%)
occurrences causally related to treatment / all	0 / 2	0 / 6	0 / 8
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 2
Lymphadenitis			
subjects affected / exposed	1 / 1647 (0.06%)	0 / 1651 (0.00%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 1647 (0.00%)	1 / 1651 (0.06%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic disorder			
subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Blindness			
subjects affected / exposed	1 / 1647 (0.06%)	0 / 1651 (0.00%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Conjunctivitis			
subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Strabismus			
subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			

Gastrointestinal disorder			
subjects affected / exposed	4 / 1647 (0.24%)	2 / 1651 (0.12%)	6 / 3298 (0.18%)
occurrences causally related to treatment / all	0 / 4	0 / 2	0 / 6
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Ileus paralytic			
subjects affected / exposed	2 / 1647 (0.12%)	0 / 1651 (0.00%)	2 / 3298 (0.06%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 2
Inguinal hernia			
subjects affected / exposed	1 / 1647 (0.06%)	0 / 1651 (0.00%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	1 / 1647 (0.06%)	0 / 1651 (0.00%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intussusception			
subjects affected / exposed	0 / 1647 (0.00%)	1 / 1651 (0.06%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal distension			
subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	3 / 1647 (0.18%)	0 / 1651 (0.00%)	3 / 3298 (0.09%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Food poisoning			

subjects affected / exposed	0 / 1647 (0.00%)	1 / 1651 (0.06%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Umbilical hernia			
subjects affected / exposed	1 / 1647 (0.06%)	0 / 1651 (0.00%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 1647 (0.00%)	1 / 1651 (0.06%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	94 / 1647 (5.71%)	67 / 1651 (4.06%)	161 / 3298 (4.88%)
occurrences causally related to treatment / all	0 / 94	0 / 67	0 / 161
deaths causally related to treatment / all	0 / 24	0 / 15	0 / 39
Pneumonia			

subjects affected / exposed	55 / 1647 (3.34%)	54 / 1651 (3.27%)	109 / 3298 (3.31%)
occurrences causally related to treatment / all	0 / 55	0 / 54	0 / 109
deaths causally related to treatment / all	0 / 14	0 / 13	0 / 27
Bronchopneumonia			
subjects affected / exposed	29 / 1647 (1.76%)	25 / 1651 (1.51%)	54 / 3298 (1.64%)
occurrences causally related to treatment / all	0 / 29	0 / 25	0 / 54
deaths causally related to treatment / all	0 / 6	0 / 5	0 / 11
Sepsis			
subjects affected / exposed	33 / 1647 (2.00%)	28 / 1651 (1.70%)	61 / 3298 (1.85%)
occurrences causally related to treatment / all	0 / 33	0 / 28	0 / 61
deaths causally related to treatment / all	0 / 10	0 / 3	0 / 13
Bronchiolitis			
subjects affected / exposed	21 / 1647 (1.28%)	17 / 1651 (1.03%)	38 / 3298 (1.15%)
occurrences causally related to treatment / all	0 / 21	0 / 17	0 / 38
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaria			
subjects affected / exposed	19 / 1647 (1.15%)	25 / 1651 (1.51%)	44 / 3298 (1.33%)
occurrences causally related to treatment / all	0 / 19	0 / 25	0 / 44
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 2
Upper respiratory tract infection			
subjects affected / exposed	7 / 1647 (0.43%)	7 / 1651 (0.42%)	14 / 3298 (0.42%)
occurrences causally related to treatment / all	0 / 7	0 / 7	0 / 14
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis			
subjects affected / exposed	7 / 1647 (0.43%)	4 / 1651 (0.24%)	11 / 3298 (0.33%)
occurrences causally related to treatment / all	0 / 7	0 / 4	0 / 11
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 2
Pneumocystis jiroveci pneumonia			
subjects affected / exposed	4 / 1647 (0.24%)	4 / 1651 (0.24%)	8 / 3298 (0.24%)
occurrences causally related to treatment / all	0 / 4	0 / 4	0 / 8
deaths causally related to treatment / all	0 / 3	0 / 3	0 / 6
Pulmonary tuberculosis			

subjects affected / exposed	3 / 1647 (0.18%)	3 / 1651 (0.18%)	6 / 3298 (0.18%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 6
deaths causally related to treatment / all	0 / 2	0 / 1	0 / 3
Lower respiratory tract infection			
subjects affected / exposed	0 / 1647 (0.00%)	2 / 1651 (0.12%)	2 / 3298 (0.06%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oral candidiasis			
subjects affected / exposed	2 / 1647 (0.12%)	1 / 1651 (0.06%)	3 / 3298 (0.09%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	2 / 1647 (0.12%)	0 / 1651 (0.00%)	2 / 3298 (0.06%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia viral			
subjects affected / exposed	3 / 1647 (0.18%)	0 / 1651 (0.00%)	3 / 3298 (0.09%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Croup infectious			
subjects affected / exposed	1 / 1647 (0.06%)	1 / 1651 (0.06%)	2 / 3298 (0.06%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			
subjects affected / exposed	2 / 1647 (0.12%)	1 / 1651 (0.06%)	3 / 3298 (0.09%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis bacterial			
subjects affected / exposed	1 / 1647 (0.06%)	1 / 1651 (0.06%)	2 / 3298 (0.06%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis pneumococcal			

subjects affected / exposed	0 / 1647 (0.00%)	2 / 1651 (0.12%)	2 / 3298 (0.06%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 2
Otitis media acute			
subjects affected / exposed	1 / 1647 (0.06%)	1 / 1651 (0.06%)	2 / 3298 (0.06%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	1 / 1647 (0.06%)	0 / 1651 (0.00%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tonsillitis			
subjects affected / exposed	2 / 1647 (0.12%)	0 / 1651 (0.00%)	2 / 3298 (0.06%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	0 / 1647 (0.00%)	2 / 1651 (0.12%)	2 / 3298 (0.06%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acquired immunodeficiency syndrome			
subjects affected / exposed	0 / 1647 (0.00%)	1 / 1651 (0.06%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Respiratory tract infection			
subjects affected / exposed	1 / 1647 (0.06%)	0 / 1651 (0.00%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Staphylococcal skin infection			
subjects affected / exposed	1 / 1647 (0.06%)	1 / 1651 (0.06%)	2 / 3298 (0.06%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Abscess			

subjects affected / exposed	0 / 1647 (0.00%)	1 / 1651 (0.06%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess neck			
subjects affected / exposed	1 / 1647 (0.06%)	0 / 1651 (0.00%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral malaria			
subjects affected / exposed	1 / 1647 (0.06%)	0 / 1651 (0.00%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eczema infected			
subjects affected / exposed	1 / 1647 (0.06%)	0 / 1651 (0.00%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Febrile infection			
subjects affected / exposed	0 / 1647 (0.00%)	1 / 1651 (0.06%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Herpes simplex			
subjects affected / exposed	1 / 1647 (0.06%)	0 / 1651 (0.00%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Klebsiella bacteremia			
subjects affected / exposed	0 / 1647 (0.00%)	1 / 1651 (0.06%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Meningitis bacterial			
subjects affected / exposed	0 / 1647 (0.00%)	1 / 1651 (0.06%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Nosocomial infection			

subjects affected / exposed	1 / 1647 (0.06%)	0 / 1651 (0.00%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 1
Parotid abscess			
subjects affected / exposed	1 / 1647 (0.06%)	0 / 1651 (0.00%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pharyngotonsillitis			
subjects affected / exposed	1 / 1647 (0.06%)	0 / 1651 (0.00%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 1647 (0.00%)	2 / 1651 (0.12%)	2 / 3298 (0.06%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative wound infection			
subjects affected / exposed	0 / 1647 (0.00%)	1 / 1651 (0.06%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection viral			
subjects affected / exposed	1 / 1647 (0.06%)	0 / 1651 (0.00%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis neonatal			
subjects affected / exposed	0 / 1647 (0.00%)	1 / 1651 (0.06%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Septic shock			
subjects affected / exposed	0 / 1647 (0.00%)	1 / 1651 (0.06%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Tuberculosis			

subjects affected / exposed	1 / 1647 (0.06%)	1 / 1651 (0.06%)	2 / 3298 (0.06%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1
Varicella			
subjects affected / exposed	1 / 1647 (0.06%)	0 / 1651 (0.00%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral tonsillitis			
subjects affected / exposed	1 / 1647 (0.06%)	0 / 1651 (0.00%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 1647 (0.06%)	0 / 1651 (0.00%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 1647 (0.00%)	1 / 1651 (0.06%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Disseminated tuberculosis			
subjects affected / exposed	0 / 1647 (0.00%)	1 / 1651 (0.06%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Empyema			
subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia urinary tract infection			
subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			

subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis tuberculous			
subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perianal abscess			
subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Keratitis herpetic			
subjects affected / exposed	1 / 1647 (0.06%)	0 / 1651 (0.00%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	1 / 1647 (0.06%)	0 / 1651 (0.00%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salmonella sepsis			
subjects affected / exposed	0 / 1647 (0.00%)	1 / 1651 (0.06%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin infection			
subjects affected / exposed	0 / 1647 (0.00%)	1 / 1651 (0.06%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess limb			
subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			

subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	3 / 1647 (0.18%)	3 / 1651 (0.18%)	6 / 3298 (0.18%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 6
deaths causally related to treatment / all	0 / 1	0 / 3	0 / 4
Kwashiorkor			
subjects affected / exposed	3 / 1647 (0.18%)	4 / 1651 (0.24%)	7 / 3298 (0.21%)
occurrences causally related to treatment / all	0 / 3	0 / 4	0 / 7
deaths causally related to treatment / all	0 / 3	0 / 2	0 / 5
Malnutrition			
subjects affected / exposed	5 / 1647 (0.30%)	0 / 1651 (0.00%)	5 / 3298 (0.15%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 2
Marasmus			
subjects affected / exposed	3 / 1647 (0.18%)	5 / 1651 (0.30%)	8 / 3298 (0.24%)
occurrences causally related to treatment / all	0 / 3	0 / 5	0 / 8
deaths causally related to treatment / all	0 / 2	0 / 3	0 / 5
Metabolic acidosis			
subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypernatraemia			
subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	0 / 1647 (0.00%)	1 / 1651 (0.06%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemic syndrome			

subjects affected / exposed	0 / 1647 (0.00%)	1 / 1651 (0.06%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cachexia			
subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrolyte imbalance			
subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemic seizure			
subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	0 / 1647 (0.00%)	1 / 1651 (0.06%)	1 / 3298 (0.03%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 1

Serious adverse events	Placebo Group		
Total subjects affected by serious adverse events			
subjects affected / exposed	246 / 1641 (14.99%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neuroblastoma			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Adenoidectomy			

subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pyrexia			
subjects affected / exposed	4 / 1641 (0.24%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 1		
Sudden infant death syndrome			
subjects affected / exposed	2 / 1641 (0.12%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Cyst			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Irritability			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sudden death			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Immune system disorders			
Immunosuppression			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		

Reproductive system and breast disorders			
Genital rash			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	2 / 1641 (0.12%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pneumonia aspiration			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Asphyxia			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aspiration			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bronchospasm			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Epistaxis			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory arrest			

subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atelectasis			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dyspnea			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Grunting			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Pneumothorax			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory distress			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Adenoidal hypertrophy			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Foreign body aspiration			

subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Thermal burn			
subjects affected / exposed	4 / 1641 (0.24%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Brachial plexus injury			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fractured skull depressed			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Head injury			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Femur fracture			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonitis chemical			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Soft tissue injury			

subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Therapeutic agent toxicity			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Chemical poisoning			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin laceration			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Drug toxicity			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Congenital, familial and genetic disorders			
Heart disease congenital			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Patent ductus arteriosus			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Phimosis			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			

Cardiac failure congestive				
subjects affected / exposed	0 / 1641 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypovolaemic shock				
subjects affected / exposed	0 / 1641 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tachycardia				
subjects affected / exposed	0 / 1641 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Febrile convulsion				
subjects affected / exposed	6 / 1641 (0.37%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	0 / 0			
Encephalitis				
subjects affected / exposed	2 / 1641 (0.12%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Status epilepticus				
subjects affected / exposed	0 / 1641 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Convulsion				
subjects affected / exposed	3 / 1641 (0.18%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 1			
Fontanelle bulging				
subjects affected / exposed	1 / 1641 (0.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hydrocephalus				

subjects affected / exposed	2 / 1641 (0.12%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Blood and lymphatic system disorders			
Anemia			
subjects affected / exposed	2 / 1641 (0.12%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Lymphadenitis			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancytopenia			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemorrhagic disorder			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Eye disorders			
Blindness			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Conjunctivitis			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Strabismus			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			

Gastrointestinal disorder			
subjects affected / exposed	3 / 1641 (0.18%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Ileus paralytic			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ileus			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intussusception			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal distension			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal obstruction			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Vomiting			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Food poisoning			

subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Umbilical hernia			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Eczema			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urticaria			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	104 / 1641 (6.34%)		
occurrences causally related to treatment / all	0 / 104		
deaths causally related to treatment / all	0 / 26		
Pneumonia			

subjects affected / exposed	64 / 1641 (3.90%)		
occurrences causally related to treatment / all	0 / 64		
deaths causally related to treatment / all	0 / 19		
Bronchopneumonia			
subjects affected / exposed	25 / 1641 (1.52%)		
occurrences causally related to treatment / all	0 / 25		
deaths causally related to treatment / all	0 / 3		
Sepsis			
subjects affected / exposed	29 / 1641 (1.77%)		
occurrences causally related to treatment / all	0 / 29		
deaths causally related to treatment / all	0 / 3		
Bronchiolitis			
subjects affected / exposed	17 / 1641 (1.04%)		
occurrences causally related to treatment / all	0 / 17		
deaths causally related to treatment / all	0 / 2		
Malaria			
subjects affected / exposed	33 / 1641 (2.01%)		
occurrences causally related to treatment / all	0 / 33		
deaths causally related to treatment / all	0 / 4		
Upper respiratory tract infection			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Meningitis			
subjects affected / exposed	2 / 1641 (0.12%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pneumocystis jiroveci pneumonia			
subjects affected / exposed	5 / 1641 (0.30%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 3		
Pulmonary tuberculosis			

subjects affected / exposed	4 / 1641 (0.24%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 2		
Lower respiratory tract infection			
subjects affected / exposed	3 / 1641 (0.18%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Oral candidiasis			
subjects affected / exposed	3 / 1641 (0.18%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	2 / 1641 (0.12%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pneumonia viral			
subjects affected / exposed	2 / 1641 (0.12%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Croup infectious			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Otitis media			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Arthritis bacterial			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Meningitis pneumococcal			

subjects affected / exposed	2 / 1641 (0.12%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Otitis media acute			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Subcutaneous abscess			
subjects affected / exposed	2 / 1641 (0.12%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Tonsillitis			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	2 / 1641 (0.12%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Acquired immunodeficiency syndrome			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Respiratory tract infection			
subjects affected / exposed	3 / 1641 (0.18%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Staphylococcal skin infection			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abscess			

subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abscess neck			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cerebral malaria			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eczema infected			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Febrile infection			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Herpes simplex			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Klebsiella bacteremia			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Meningitis bacterial			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nosocomial infection			

subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Parotid abscess			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pharyngotonsillitis			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia bacterial			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Postoperative wound infection			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection viral			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis neonatal			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Septic shock			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tuberculosis			

subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Varicella			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Viral tonsillitis			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cellulitis			
subjects affected / exposed	2 / 1641 (0.12%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Disseminated tuberculosis			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Empyema			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Escherichia urinary tract infection			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infection			

subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Meningitis tuberculous			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Perianal abscess			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Keratitis herpetic			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory syncytial virus bronchiolitis			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Salmonella sepsis			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin infection			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abscess limb			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Influenza			

subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	2 / 1641 (0.12%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 1		
Kwashiorkor			
subjects affected / exposed	8 / 1641 (0.49%)		
occurrences causally related to treatment / all	0 / 8		
deaths causally related to treatment / all	0 / 1		
Malnutrition			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Marasmus			
subjects affected / exposed	4 / 1641 (0.24%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 3		
Metabolic acidosis			
subjects affected / exposed	3 / 1641 (0.18%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Hypernatraemia			
subjects affected / exposed	2 / 1641 (0.12%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyponatraemic syndrome			

subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cachexia			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Electrolyte imbalance			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Hypoglycaemic seizure			
subjects affected / exposed	1 / 1641 (0.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemia			
subjects affected / exposed	0 / 1641 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Rotarix 2-dose Group	Rotarix 3-dose Group	Rotarix pooled Group
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 1647 (0.00%)	0 / 1651 (0.00%)	0 / 3298 (0.00%)

Non-serious adverse events	Placebo Group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 1641 (0.00%)		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
24 August 2005	This protocol was amended to implement the following changes: - To increase the sample size: The assumed attack rate of 2% for severe RV GE for sample size estimation in the original protocol was found to be too optimistic based on the results obtained in several studies with GSK Biologicals' HRV vaccine. A more conservative attack rate of 1.5% was therefore considered and the sample size was revised. - In the context of the increased sample size, to specify the target enrolment in South Africa. - To allow HIV testing according to the national guidelines in south Africa. HIV testing will be performed at Visit 3 in all subjects whose parents/guardians gave consent, followed by a confirmatory test at Visit 4 in HIV positive subjects who are asymptomatic. - To add an additional study visit to communicate results of the confirmatory HIV test to the parents/guardians. - To change method of data collection from Remote Data Entry to Case Report Forms. - Following feedback from the ERCs, changes to reflect local clinical practice for care and treatment were made.
02 August 2007	This amendment was done on 2 August 2007 to implement the following changes for the South Africa cohort as recommended by the Rotavirus Vaccine Program (RVP) organization which co-sponsors this study. - To perform an interim analysis on efficacy data collected from Cohort 1 and Cohort 2 in South Africa until the cut off date of 31 August 2007. This interim analysis is performed under the request by RVP to allow early review of African efficacy data to prepare implementation of universal mass vaccination (UMV) in some African countries. The availability of earlier results suggesting favorable efficacy of the vaccine in developing countries in Africa would be useful as an advocacy tool to stimulate policy makers both at global level (e.g. WHO, SAGE, GAVI) and at the country level to prepare for accelerated decision-making and introduction activities in Africa. - To extend follow-up for efficacy until the end of the second consecutive RV season for Cohort 2 South Africa. Also, safety follow-up for SAEs and AEs leading to drop out will be performed for these subjects until the end of the RV season. The follow-up during the second year will also be performed for the cohort in Malawi. Additional follow-up may allow for the estimation of vaccine efficacy, either among all infants over the combined first and second year of life or during the second year of life. Additional follow-up may also provide greater power to investigate other aspects of vaccine efficacy such as protection among infants in these populations with high HIV prevalence, better estimation of strain and dose-specific vaccine efficacy. - To implement a supplementary ICF to allow using post-breast feeding cessation HIV results in the analysis when HIV test is performed.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported