



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 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) | 0 0 0 0 0 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 standard deviation | 6.4 ± 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

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 | <p>This protocol was amended to implement the following changes:</p> <ul style="list-style-type: none">- 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 | <p>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.</p> <ul style="list-style-type: none">- 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