



Clinical trial results:

A phase III, observer-blind, randomized, multi-country, non-influenza vaccine comparator-controlled study to demonstrate the efficacy of GlaxoSmithKline Biologicals' quadrivalent seasonal influenza candidate vaccine GSK2321138A (FLU D-QIV), administered intramuscularly in children 6 to 35 months of age.

Summary

| | |
|--------------------------|-------------------------------|
| EudraCT number | 2011-000758-41 |
| Trial protocol | CZ ES BE GB PL Outside EU/EEA |
| Global end of trial date | 31 December 2014 |

Results information

| | |
|--------------------------------|-------------------|
| Result version number | v2 (current) |
| This version publication date | 14 September 2018 |
| First version publication date | 07 January 2017 |
| Version creation reason | |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | 115345 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01439360 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | GlaxoSmithKline Biologicals |
| Sponsor organisation address | Rue de l'Institut 89,, Rixensart,, Belgium, |
| Public contact | Clinical Trials Call Center,, GlaxoSmithKline Biologicals, 44 2089-904466, GSKClinicalSupportHD@gsk.com |
| Scientific contact | Clinical Trials Call Center,, GlaxoSmithKline Biologicals, 44 2089-904466, GSKClinicalSupportHD@gsk.com |

Notes:

Paediatric regulatory details

| | |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMA-000817-PIP02-11 |
| 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 | 13 July 2016 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 31 December 2014 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

- To evaluate the efficacy of FLU D-QIV in the prevention of RT-PCR confirmed moderate to severe influenza A and/or B disease due to any seasonal influenza strain, when compared to non-influenza vaccine controls in children aged 6 to 35 months.
- To evaluate the efficacy of FLU D-QIV in the prevention of RT-PCR confirmed influenza A and/or B disease due to any seasonal influenza strain, when compared to non-influenza vaccine controls in children aged 6 to 35 months.

Protection of trial subjects:

All subjects were observed closely for at least 30 minutes following the administration of the vaccine(s)/placebo, with appropriate medical treatment readily available in case of anaphylaxis.

Background therapy: -

Evidence for comparator: -

| | |
|---|-----------------|
| Actual start date of recruitment | 01 October 2011 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------------|
| Country: Number of subjects enrolled | Bangladesh: 2911 |
| Country: Number of subjects enrolled | Belgium: 147 |
| Country: Number of subjects enrolled | Czech Republic: 416 |
| Country: Number of subjects enrolled | Dominican Republic: 1962 |
| Country: Number of subjects enrolled | Honduras: 1314 |
| Country: Number of subjects enrolled | India: 465 |
| Country: Number of subjects enrolled | Lebanon: 250 |
| Country: Number of subjects enrolled | Philippines: 1448 |
| Country: Number of subjects enrolled | Poland: 1266 |
| Country: Number of subjects enrolled | Spain: 858 |
| Country: Number of subjects enrolled | Thailand: 602 |
| Country: Number of subjects enrolled | Turkey: 37 |
| Country: Number of subjects enrolled | United Kingdom: 370 |
| Worldwide total number of subjects | 12046 |
| EEA total number of subjects | 3057 |

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) | 6445 |
| Children (2-11 years) | 5601 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details: -

Pre-assignment period milestones

| | |
|----------------------------|-------|
| Number of subjects started | 12046 |
|----------------------------|-------|

| | |
|------------------------------|-------|
| Number of subjects completed | 12018 |
|------------------------------|-------|

Pre-assignment subject non-completion reasons

| | |
|----------------------------|-----------------|
| Reason: Number of subjects | Invalid ICF: 21 |
|----------------------------|-----------------|

| | |
|----------------------------|--|
| Reason: Number of subjects | Vaccine not administered subject number allocated: 7 |
|----------------------------|--|

Period 1

| | |
|----------------|--------------------------------|
| Period 1 title | Overall Study (overall period) |
|----------------|--------------------------------|

| | |
|------------------------------|-----|
| Is this the baseline period? | Yes |
|------------------------------|-----|

| | |
|-------------------|-------------------------|
| Allocation method | Randomised - controlled |
|-------------------|-------------------------|

| | |
|---------------|--------------|
| Blinding used | Double blind |
|---------------|--------------|

| | |
|---------------|---|
| Roles blinded | Subject, Investigator, Monitor, Data analyst, Carer, Assessor |
|---------------|---|

Blinding implementation details:

Data will be collected in an observer-blind manner. The laboratory in charge of the laboratory testing was blinded to the treatment, and codes were used to link the subject and study (without any link to the treatment attributed to the subject) to each sample.

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|-----------|-------|
| Arm title | D-QIV |
|-----------|-------|

Arm description:

Subjects received 1 or 2 doses of candidate influenza Influsplit™ Tetra vaccine (GSK2321138A).

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|---------------------------|
| Investigational medicinal product name | Influsplit™ Tetra (D-QIV) |
|--|---------------------------|

| | |
|--|--|
| Investigational medicinal product code | |
|--|--|

| | |
|------------|-----------------------------|
| Other name | Fluarix™ Tetra, GSK2321138A |
|------------|-----------------------------|

| | |
|----------------------|--------------------------|
| Pharmaceutical forms | Suspension for injection |
|----------------------|--------------------------|

| | |
|--------------------------|-------------------|
| Routes of administration | Intramuscular use |
|--------------------------|-------------------|

Dosage and administration details:

1 or 2 doses administered intramuscularly at Day 0 (primed subjects) and Days 0 and 28 (unprimed subjects)

| | |
|-----------|---------|
| Arm title | Control |
|-----------|---------|

Arm description:

In function of their age and D-QIV-vaccine status, subjects received Prevenar 13® or Havrix® Junior and possibly a varicella vaccine (Varilrix® or Varivax/ProVarivax ®).

| | |
|----------|-------------------|
| Arm type | Active comparator |
|----------|-------------------|

| | |
|--|--------------|
| Investigational medicinal product name | Prevenar 13® |
|--|--------------|

| | |
|--|--|
| Investigational medicinal product code | |
|--|--|

| | |
|------------|---|
| Other name | Pfizer's pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed) (PCV-13) |
|------------|---|

| | |
|----------------------|--------------------------|
| Pharmaceutical forms | Suspension for injection |
|----------------------|--------------------------|

| | |
|--------------------------|-------------------|
| Routes of administration | Intramuscular use |
|--------------------------|-------------------|

Dosage and administration details:

-2 doses administered at Days 0 and 28 and 1 booster dose at study completion (Day 180 approximately), according to the prescribing information for subjects < 12 months of age.

| | |
|--|---|
| Investigational medicinal product name | Varivax® |
| Investigational medicinal product code | SUB25312 |
| Other name | ProVarivax® |
| Pharmaceutical forms | Powder and solvent for suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

1 dose administered (depending on the licensed vaccine in the participating country) at Day 0 in unprimed subjects ≥12 months of age.

| | |
|--|---|
| Investigational medicinal product name | Varilrix® |
| Investigational medicinal product code | SUB20954 |
| Other name | |
| Pharmaceutical forms | Powder and solvent for solution for injection |
| Routes of administration | Subcutaneous use |

Dosage and administration details:

1 dose administered subcutaneously (depending on the licensed vaccine in the participating country) at Day 0 in unprimed subjects ≥12 months of age.

| | |
|--|--------------------------|
| Investigational medicinal product name | Havrix® |
| Investigational medicinal product code | SUB25294 |
| Other name | Havrix® Junior |
| Pharmaceutical forms | Suspension for injection |
| Routes of administration | Intramuscular use |

Dosage and administration details:

1 dose administered intramuscularly at Day 0 and booster dose at study completion (Day 180 approximately)

| Number of subjects in period 1^[1] | D-QIV | Control |
|---|--------------|----------------|
| Started | 6006 | 6012 |
| Completed | 5808 | 5804 |
| Not completed | 198 | 208 |
| Consent withdrawn by subject | 140 | 129 |
| Others | 10 | 5 |
| Adverse event, non-fatal | 4 | 16 |
| Lost to follow-up | 43 | 58 |
| Protocol deviation | 1 | - |

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: Out of the 12046 enrolled subjects, 21 subjects were excluded from all statistical analyses due to an invalid informed consent form (ICF), 7 subjects did not receive any study vaccine despite being allocated a subject number.

Baseline characteristics

Reporting groups

| | |
|---|---------|
| Reporting group title | D-QIV |
| Reporting group description: | |
| Subjects received 1 or 2 doses of candidate influenza Influsplit™ Tetra vaccine (GSK2321138A). | |
| Reporting group title | Control |
| Reporting group description: | |
| In function of their age and D-QIV-vaccine status, subjects received Prevenar 13® or Havrix® Junior and possibly a varicella vaccine (Varilrix® or Varivax/ProVarivax ®). | |

| Reporting group values | D-QIV | Control | Total |
|------------------------|-------|---------|-------|
| Number of subjects | 6006 | 6012 | 12018 |
| Age categorical | | | |
| Units: Subjects | | | |

| | | | |
|---|-------|-------|------|
| Age continuous | | | |
| Units: months | | | |
| arithmetic mean | 21.9 | 21.8 | |
| standard deviation | ± 8.0 | ± 8.0 | - |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 2933 | 2925 | 5858 |
| Male | 3073 | 3087 | 6160 |
| Race/Ethnicity, Customized | | | |
| Units: Subjects | | | |
| African Heritage / African American | 24 | 20 | 44 |
| Asian - Central/South Asian Heritage | 1062 | 1053 | 2115 |
| Asian - East Asian Heritage | 2 | 0 | 2 |
| Asian - Japanese Heritage | 2 | 0 | 2 |
| Asian - South East Asian Heritage | 1661 | 1666 | 3327 |
| Native Hawaiian or Other Pacific Islander | 3 | 0 | 3 |
| Other | 1639 | 1642 | 3281 |
| White - Arabic / North African Heritage | 142 | 149 | 291 |
| White - Caucasian / European Heritage | 1471 | 1482 | 2953 |

End points

End points reporting groups

| | |
|---|---------|
| Reporting group title | D-QIV |
| Reporting group description: Subjects received 1 or 2 doses of candidate influenza Influsplit™ Tetra vaccine (GSK2321138A). | |
| Reporting group title | Control |
| Reporting group description: In function of their age and D-QIV-vaccine status, subjects received Prevenar 13® or Havrix® Junior and possibly a varicella vaccine (Varilrix® or Varivax/ProVarivax ®). | |

Primary: Number of subjects with moderate to severe RT-PCR confirmed influenza.

| | |
|---|--|
| End point title | Number of subjects with moderate to severe RT-PCR confirmed influenza. |
| End point description: Attack rate (AR) was defined as the number/percentage of subjects with at least 1 RT-PCR confirmed influenza event. | |
| End point type | Primary |
| End point timeframe: During the surveillance period (approximately 6 to 8 months) | |

| End point values | D-QIV | Control | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 5707 | 5697 | | |
| Units: Subjects | 90 | 242 | | |

Statistical analyses

| | |
|--|------------------------|
| Statistical analysis title | Statistical analysis 1 |
| Statistical analysis description: The efficacy of the D-QIV vaccine would be demonstrated if the LL of the two-sided 97.5% CI for vaccine efficacy (VE) is above (>) 25%. | |
| Comparison groups | D-QIV v Control |
| Number of subjects included in analysis | 11404 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Regression, Cox |
| Parameter estimate | Vaccine efficacy (VE) |
| Point estimate | 63.2 |
| Confidence interval | |
| level | Other: 97.5 % |
| sides | 2-sided |
| lower limit | 51.8 |
| upper limit | 72.3 |

Primary: Number of subjects with RT-PCR confirmed influenza of any severity.

| | |
|-----------------|---|
| End point title | Number of subjects with RT-PCR confirmed influenza of any severity. |
|-----------------|---|

End point description:

Attack rate (AR) was defined as the number/percentage of subjects with at least 1 RT-PCR confirmed influenza event.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

During the surveillance period (approximately 6 to 8 months)

| End point values | D-QIV | Control | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 5707 | 5697 | | |
| Units: Subjects | 344 | 662 | | |

Statistical analyses

| | |
|----------------------------|------------------------|
| Statistical analysis title | Statistical analysis 1 |
|----------------------------|------------------------|

Statistical analysis description:

The efficacy of the D-QIV vaccine would be demonstrated if the LL of the two-sided 97.5% CI for VE is above 15%.

| | |
|---|-----------------------|
| Comparison groups | D-QIV v Control |
| Number of subjects included in analysis | 11404 |
| Analysis specification | Pre-specified |
| Analysis type | |
| Method | Regression, Cox |
| Parameter estimate | Vaccine efficacy (VE) |
| Point estimate | 49.8 |
| Confidence interval | |
| level | Other: 97.5 % |
| sides | 2-sided |
| lower limit | 41.8 |
| upper limit | 56.8 |

Secondary: Number of subjects with first occurrence of lower respiratory illness (LRI) with RT-PCR confirmed influenza.

| | |
|-----------------|--|
| End point title | Number of subjects with first occurrence of lower respiratory illness (LRI) with RT-PCR confirmed influenza. |
|-----------------|--|

End point description:

Attack rate (AR) was defined as the number/percentage of subjects with at least 1 RT-PCR confirmed influenza event.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At any time starting 7 days before the onset of LRI and ending 7 days after end of LRI during the surveillance period (approximately 6 to 8 months)

| End point values | D-QIV | Control | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 5707 | 5697 | | |
| Units: Subjects | 28 | 61 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with first occurrence of culture-confirmed moderate to severe influenza A and/or B disease due to antigenically-matching influenza strains.

| | |
|-----------------|--|
| End point title | Number of subjects with first occurrence of culture-confirmed moderate to severe influenza A and/or B disease due to antigenically-matching influenza strains. |
|-----------------|--|

End point description:

Attack rate (AR) was defined as the number/percentage of subjects with at least 1 RT-PCR confirmed influenza event.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

During the surveillance period (approximately 6 to 8 months)

| End point values | D-QIV | Control | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 5707 | 5697 | | |
| Units: Subjects | 20 | 88 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with first occurrence of culture-confirmed influenza A and/or B disease of any severity due to antigenically-matching influenza strains

| | |
|-----------------|--|
| End point title | Number of subjects with first occurrence of culture-confirmed influenza A and/or B disease of any severity due to antigenically-matching influenza strains |
|-----------------|--|

End point description:

Attack rate (AR) was defined as the number/percentage of subjects with at least 1 RT-PCR confirmed influenza event.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| During the surveillance period (approximately 6 to 8 months) | |

| End point values | D-QIV | Control | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 5707 | 5697 | | |
| Units: Subjects | 88 | 216 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with first occurrence of culture-confirmed moderate to severe influenza A and/or B disease due to any seasonal influenza strain.

| | |
|-----------------|---|
| End point title | Number of subjects with first occurrence of culture-confirmed moderate to severe influenza A and/or B disease due to any seasonal influenza strain. |
|-----------------|---|

End point description:

Attack rate (AR) was defined as the number/percentage of subjects with at least 1 RT-PCR confirmed influenza event.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

During the surveillance period (approximately 6 to 8 months)

| End point values | D-QIV | Control | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 5707 | 5697 | | |
| Units: Subjects | 79 | 216 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with first occurrence of culture-confirmed influenza A and/or B disease of any severity due to any seasonal influenza strain.

| | |
|-----------------|--|
| End point title | Number of subjects with first occurrence of culture-confirmed influenza A and/or B disease of any severity due to any seasonal influenza strain. |
|-----------------|--|

End point description:

Attack rate (AR) was defined as the number/percentage of subjects with at least 1 RT-PCR confirmed influenza event.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| During the surveillance period (approximately 6 to 8 months) | |

| End point values | D-QIV | Control | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 5707 | 5697 | | |
| Units: Subjects | 303 | 602 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with first occurrence of acute otitis media (AOM) with RT-PCR confirmed influenza A and/or B infection due to any seasonal influenza strain.

| | |
|-----------------|---|
| End point title | Number of subjects with first occurrence of acute otitis media (AOM) with RT-PCR confirmed influenza A and/or B infection due to any seasonal influenza strain. |
|-----------------|---|

End point description:

Attack rate (AR) was defined as the number/percentage of subjects with at least 1 RT-PCR confirmed influenza event.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At any time starting 7 days before the onset of LRI and ending 7 days after end of LRI during the surveillance period (approximately 6 to 8 months)

| End point values | D-QIV | Control | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 5707 | 5697 | | |
| Units: Subjects | 12 | 28 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects with first occurrence of RT-PCR confirmed severe influenza A and/or B due to any seasonal influenza strain.

| | |
|-----------------|--|
| End point title | Number of subjects with first occurrence of RT-PCR confirmed severe influenza A and/or B due to any seasonal influenza strain. |
|-----------------|--|

End point description:

Attack rate (AR) was defined as the number/percentage of subjects with at least 1 RT-PCR confirmed

influenza event.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| During the surveillance period (approximately 6 to 8 months) | |

| End point values | D-QIV | Control | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 5707 | 5697 | | |
| Units: Subjects | 2 | 3 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Humoral immune response in terms of haemagglutination-inhibition (HI) antibody titres against each of four vaccine strains contained in the D-QIV (in immuno subcohort of subjects only)

| | |
|-----------------|--|
| End point title | Humoral immune response in terms of haemagglutination-inhibition (HI) antibody titres against each of four vaccine strains contained in the D-QIV (in immuno subcohort of subjects only) |
|-----------------|--|

End point description:

Titers were expressed as geometric mean antibody titers (GMTs). The vaccine strains assessed were A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2), B/Brisbane/60/2008 (Victoria) and B/Brisbane/3/2007 (Yamagata). PRE= Pre-vaccination at Day 0; POST = Post-vaccination 1 at Day 28 for primed subjects or post-vaccination 2 at Day 56 for unprimed subjects

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| At Days 0 and 28/56 | |

| End point values | D-QIV | Control | | |
|--|------------------------|---------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 753 | 579 | | |
| Units: Titers | | | | |
| geometric mean (confidence interval 95%) | | | | |
| H1N1, PRE [N=744, 567] | 11.9 (10.6 to 13.2) | 11.9 (10.5 to 13.5) | | |
| H1N1, POST [N=752, 578] | 165.3 (148.6 to 183.8) | 12.6 (11.1 to 14.3) | | |
| H3N2, PRE [N=746,568] | 14.8 (13.2 to 16.5) | 13.4 (11.8 to 15.2) | | |
| H3N2, POST [N=753,578] | 132.1 (119.1 to 146.5) | 14.7 (12.9 to 16.7) | | |
| Victoria, PRE [N=745,567] | 10.0 (9.1 to 11.0) | 9.2 (8.3 to 10.1) | | |

| | | | | |
|----------------------------|------------------------|-------------------|--|--|
| Victoria, POST [N=750,579] | 92.6 (82.3 to 104.1) | 9.2 (8.4 to 10.1) | | |
| Yamagata, PRE [N=745,568] | 7.3 (6.8 to 7.8) | 7.3 (6.8 to 7.9) | | |
| Yamagata, POST [N=753,579] | 121.4 (110.1 to 133.8) | 7.6 (7.0 to 8.3) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seropositive subjects for HI antibodies against each of the 4 influenza strains contained in the D-QIV vaccine (in immuno subcohort of subjects only)

| | |
|--|---|
| End point title | Number of seropositive subjects for HI antibodies against each of the 4 influenza strains contained in the D-QIV vaccine (in immuno subcohort of subjects only) |
| End point description: | |
| A seropositive subject was a subject whose HI antibody titer was greater than or equal to the assay cut-off value of 1:10. The vaccine strains assessed were A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2), B/Brisbane/60/2008 (Victoria) and B/Brisbane/3/2007 (Yamagata). PRE= Pre-vaccination at Day 0; POST = Post-vaccination 1 at Day 28 for primed subjects or post-vaccination 2 at Day 56 for unprimed subjects. | |
| End point type | Secondary |
| End point timeframe: | |
| At Day 0 and Day 28/56 | |

| End point values | D-QIV | Control | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 753 | 579 | | |
| Units: Subjects | | | | |
| H1N1, PRE | 200 | 152 | | |
| H1N1, POST | 728 | 170 | | |
| H3N2, PRE | 266 | 187 | | |
| H3N2, POST | 740 | 210 | | |
| Victoria, PRE | 205 | 138 | | |
| Victoria, POST | 701 | 147 | | |
| Yamagata, PRE | 134 | 93 | | |
| Yamagata, POST | 719 | 108 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroconverted subjects for HI antibodies against each of the 4 influenza strains contained in the D-QIV vaccine (in immuno subcohort of subjects only)

| | |
|-----------------|--|
| End point title | Number of seroconverted subjects for HI antibodies against |
|-----------------|--|

each of the 4 influenza strains contained in the D-QIV vaccine (in immuno subcohort of subjects only)

End point description:

Seroconversion rate (SCR) was defined as the number of subjects who have either a pre-vaccination reciprocal HI titer < 1:10 and a post-vaccination reciprocal titer ≥ 1:40, or a pre-vaccination reciprocal HI titer ≥ 10 and at least a 4 fold increase in post vaccination reciprocal titer against the vaccine virus. PRE= Pre-vaccination at Day 0; POST = Post-vaccination 1 at Day 28 for primed subjects or post-vaccination 2 at Day 56 for unprimed subjects

End point type Secondary

End point timeframe:

At Day 28/56 (POST)

| End point values | D-QIV | Control | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 746 | 568 | | |
| Units: Subjects | | | | |
| H1N1 | 596 | 20 | | |
| H3N2 | 513 | 24 | | |
| Victoria | 514 | 5 | | |
| Yamagata | 605 | 13 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Mean geometric increase (MGI) for HI antibody titer against each of the 4 vaccine influenza strains contained in the D-QIV vaccine (in immuno subcohort of subjects only).

End point title Mean geometric increase (MGI) for HI antibody titer against each of the 4 vaccine influenza strains contained in the D-QIV vaccine (in immuno subcohort of subjects only).

End point description:

MGI also known as the seroconversion factor [SCF] was defined as the fold increase in serum HI GMTs post vaccination compared to pre-vaccination (Day 0). The vaccine strains assessed were A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2), B/Brisbane/60/2008 (Victoria) and B/Brisbane/3/2007 (Yamagata). POST = Post-vaccination 1 at Day 28 for primed subjects or post-vaccination 2 at Day 56 for unprimed subjects.

End point type Secondary

End point timeframe:

At Day 28/56 (POST)

| End point values | D-QIV | Control | | |
|--|---------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 746 | 568 | | |
| Units: Fold change | | | | |
| geometric mean (confidence interval 95%) | | | | |
| H1N1 | 14 (12.8 to 15.3) | 1.1 (1.0 to 1.1) | | |
| H3N2 | 9.0 (8.2 to 9.8) | 1.1 (1.0 to 1.2) | | |
| Victoria | 9.3 (8.6 to 10.2) | 1.0 (1.0 to 1.1) | | |
| Yamagata | 16.7 (15.2 to 18.3) | 1.1 (1.0 to 1.1) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of seroprotected subjects for HI antibodies against each of the 4 influenza strains contained in the D-QIV vaccine (in immuno subcohort of subjects only)

| | |
|-----------------|--|
| End point title | Number of seroprotected subjects for HI antibodies against each of the 4 influenza strains contained in the D-QIV vaccine (in immuno subcohort of subjects only) |
|-----------------|--|

End point description:

Seroprotection rate (SPR) was defined as the number of subjects with H1N1 reciprocal HI titers $\geq 1:40$ against the tested vaccine virus. The vaccine strains assessed were A/California/7/2009 (H1N1), A/Victoria/210/2009 (H3N2), B/Brisbane/60/2008 (Victoria) and B/Brisbane/3/2007 (Yamagata). PRE= Pre-vaccination at Day 0; POST = Post-vaccination 1 at Day 28 for primed subjects or post-vaccination 2 at Day 56 for unprimed subjects

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

At Day 0 and Day 28/56

| End point values | D-QIV | Control | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 753 | 579 | | |
| Units: Subjects | | | | |
| H1N1, PRE | 182 | 134 | | |
| H1N1, POST | 640 | 146 | | |
| H3N2, PRE | 238 | 159 | | |
| H3N2, POST | 612 | 175 | | |
| Victoria, PRE | 143 | 103 | | |
| Victoria, POST | 539 | 101 | | |
| Yamagata, PRE | 73 | 59 | | |
| Yamagata, POST | 638 | 64 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any and grade 3 solicited local symptoms.

| | |
|-----------------|--|
| End point title | Number of subjects reporting any and grade 3 solicited local symptoms. |
|-----------------|--|

End point description:

Solicited local symptoms assessed were pain, redness and swelling. Any was defined as any solicited local symptom reported irrespective of intensity. Grade 3 pain was defined as pain that resulted crying when limb was moved/ spontaneously painful. Grade 3 redness and swelling was greater than 50 millimeters (mm) i.e. >50mm.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

During the 7-day post-vaccination period (Days 0-6 for Dose 1, Days 28-34 for Dose 2)

| End point values | D-QIV | Control | | |
|--|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 5907 | 5901 | | |
| Units: Subjects | | | | |
| Any Pain, Dose 1 [N=5899, 5896] | 1015 | 1047 | | |
| Grade 3 Pain, Dose 1 [N=5899, 5896] | 23 | 30 | | |
| Any Redness, Dose 1 [N=5899, 5896] | 775 | 831 | | |
| Grade 3 Redness, Pain, Dose 1 [N=5899, 5896] | 1 | 0 | | |
| Any Swelling, Dose 1 [N=5899, 5896] | 467 | 518 | | |
| Grade 3 Swelling, Dose 1 [N=5899, 5896] | 0 | 0 | | |
| Any Pain, Dose 2 [N=5757, 5766] | 808 | 820 | | |
| Grade 3 Pain, Dose 2 [N=5757, 5766] | 21 | 21 | | |
| Any Redness, Dose 2 [N=5757, 5766] | 587 | 631 | | |
| Grade 3 Redness, Dose 2 [N=5757, 5766] | 2 | 0 | | |
| Any Swelling, Dose 2 [N=5757, 5766] | 375 | 409 | | |
| Grade 3 Swelling, Dose 2 [N=5757, 5766] | 2 | 3 | | |
| Any Pain, Across doses [N=5907,5901] | 1350 | 1375 | | |
| Grade 3 Pain, Across doses [N=5907,5901] | 42 | 48 | | |
| Any Redness, Across doses [N=5907,5901] | 980 | 1091 | | |
| Grade 3 Redness, Across doses [N=5907,5901] | 3 | 0 | | |
| Any Swelling, Across doses [N=5907,5901] | 665 | 742 | | |

| | | | | |
|---|---|---|--|--|
| Grade 3 Swelling, Across doses [N=5907,5901] | 2 | 3 | | |
|---|---|---|--|--|

Statistical analyses

No statistical analyses for this end point

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

| | |
|-----------------|---|
| End point title | Number of subjects reporting any, grade 3 and related solicited general symptoms. |
|-----------------|---|

End point description:

Solicited general symptoms assessed were Drowsiness, Irritability/fussiness, Loss of appetite and Temperature (Axillary). Any was defined as any general symptom reported irrespective of intensity or relationship to vaccination. Grade 3 was defined as symptoms that prevented normal activity. Related was defined as general symptom assessed by the investigator to have a causal relationship to vaccination.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

During the 7-day post-vaccination period (Days 0-6 for Dose 1, Days 28-34 for Dose 2)

| End point values | D-QIV | Control | | |
|---|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 5908 | 5901 | | |
| Units: Subjects | | | | |
| Any Drowsiness, Dose 1 [N=5898, 5896] | 739 | 829 | | |
| Grade 3 Drowsiness, Dose 1 [N=5898, 5896] | 39 | 52 | | |
| Related Drowsiness, Dose 1 [N=5898, 5896] | 490 | 535 | | |
| Any Irritability, Dose 1 [N=5898, 5896] | 955 | 1029 | | |
| Grade 3 Irritability, Dose 1 [N=5898, 5896] | 42 | 62 | | |
| Related Irritability, Dose 1 [N=5898, 5896] | 617 | 669 | | |
| Any Loss of appetite, Dose 1 [N=5898, 5896] | 847 | 872 | | |
| Grade 3 Loss of appetite, Dose 1 [N=5898, 5896] | 68 | 60 | | |
| Related Loss of appetite, Dose 1 [N=5898, 5896] | 541 | 523 | | |
| Any Fever, Dose 1 [N=5898, 5896] | 372 | 425 | | |
| Grade 3 Fever, Dose 1 [N=5898, 5896] | 78 | 76 | | |
| Related Fever, Dose 1 [N=5898, 5896] | 243 | 287 | | |
| Any Drowsiness, Dose 2 [N=5755, 5762] | 519 | 558 | | |
| Grade 3 Drowsiness, Dose 2 [N=5755, 5762] | 25 | 24 | | |

| | | | | |
|--|------|------|--|--|
| Related Drowsiness, Dose 2 [N=5755, 5762] | 324 | 361 | | |
| Any Irritability, Dose 2 [N=5755, 5762] | 777 | 777 | | |
| Grade 3 Irritability, Dose 2 [N=5755, 5762] | 36 | 52 | | |
| Related Irritability, Dose 2 [N=5755, 5762] | 488 | 495 | | |
| Any Loss of appetite, Dose 2 [N=5755, 5762] | 652 | 681 | | |
| Grade 3 Loss of appetite, Dose 2 [N=5755, 5762] | 47 | 44 | | |
| Related Loss of appetite, Dose 2 [N=5755, 5762] | 378 | 413 | | |
| Any Fever, Dose 2 [N=5755, 5762] | 336 | 363 | | |
| Grade 3 Fever, Dose 2 [N=5755, 5762] | 65 | 70 | | |
| Related Fever, Dose 2 [N=5755, 5762] | 195 | 215 | | |
| Any Drowsiness, Across Doses [N=5908, 5901] | 1024 | 1129 | | |
| Grade 3 Drowsiness, Across Doses [N=5908, 5901] | 61 | 73 | | |
| Related Drowsiness, Across Doses [N=5908, 5901] | 673 | 738 | | |
| Any Irritability, Across Doses [N=5908, 5901] | 1383 | 1427 | | |
| Grade 3 Irritability, Across Doses [N=5908, 5901] | 77 | 107 | | |
| Related Irritability, Across Doses [N=5908, 5901] | 905 | 940 | | |
| Any Loss of appetite, Across Doses [N=5908, 5901] | 1227 | 1288 | | |
| Grade3 Loss of appetite,Across Doses[N=5908, 5901] | 111 | 97 | | |
| Related Loss of appetite,AcrossDoses[N=5908, 5901] | 774 | 809 | | |
| Any Fever, Across Doses [N=5908, 5901] | 659 | 732 | | |
| Grade 3 Fever, Across Doses [N=5908, 5901] | 137 | 141 | | |
| Related Fever, Across Doses [N=5908, 5901] | 413 | 476 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of solicited local symptoms

| | |
|---|--------------------------------------|
| End point title | Duration of solicited local symptoms |
| End point description: | |
| Duration was defined as number of days with any grade of local symptoms. | |
| End point type | Secondary |
| End point timeframe: | |
| During the 7-day post-vaccination period (Days 0-6 for Dose 1, Days 28-34 for Dose 2) | |

| End point values | D-QIV | Control | | |
|-------------------------------|------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 1015 | 1047 | | |
| Units: Days | | | | |
| median (full range (min-max)) | | | | |
| Pain, Dose 1 [N=1015,1047] | 1.0 (1.0 to 2.0) | 1.0 (1.0 to 2.0) | | |
| Pain, Dose 2 [N=808,820] | 1.0 (1.0 to 2.0) | 1.0 (1.0 to 2.0) | | |
| Redness, Dose 1 [N=775,831] | 2.0 (1.0 to 3.0) | 2.0 (1.0 to 3.0) | | |
| Redness, Dose 2 [N=587,631] | 2.0 (1.0 to 3.0) | 2.0 (1.0 to 3.0) | | |
| Swelling, Dose 1 [N=467,518] | 2.0 (1.0 to 3.0) | 2.0 (1.0 to 3.0) | | |
| Swelling, Dose 2 [N=375,409] | 1.0 (1.0 to 2.0) | 2.0 (1.0 to 2.0) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of solicited general symptoms

| | |
|---|--|
| End point title | Duration of solicited general symptoms |
| End point description: | |
| Duration was defined as number of days with any grade of general symptoms. | |
| End point type | Secondary |
| End point timeframe: | |
| During the 7-day post-vaccination period (Days 0-6 for Dose 1, Days 28-34 for Dose 2) | |

| End point values | D-QIV | Control | | |
|--------------------------------------|------------------|------------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 955 | 1029 | | |
| Units: Days | | | | |
| median (full range (min-max)) | | | | |
| Drowsiness, Dose 1 [N=739,829] | 2.0 (1.0 to 3.0) | 2.0 (1.0 to 3.0) | | |
| Drowsiness, Dose 2 [N=519,558] | 2.0 (1.0 to 3.0) | 2.0 (1.0 to 3.0) | | |
| Irritability, Dose 1 [N=955,1029] | 2.0 (1.0 to 3.0) | 2.0 (1.0 to 3.0) | | |
| Irritability, Dose 2 [N=777,777] | 2.0 (1.0 to 3.0) | 2.0 (1.0 to 3.0) | | |
| Loss of appetite, Dose 1 [N=847,872] | 2.0 (1.0 to 4.0) | 2.0 (1.0 to 4.0) | | |
| Loss of appetite, Dose 2 [N=652,681] | 3.0 (2.0 to 4.0) | 2.0 (1.0 to 4.0) | | |
| Fever, Dose 1 [N=390,438] | 1.0 (1.0 to 2.0) | 1.0 (1.0 to 2.0) | | |
| Fever, Dose 2 [N=347,372] | 2.0 (1.0 to 3.0) | 1.0 (1.0 to 3.0) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any, grade 3 and related unsolicited adverse events (AEs)

| | |
|-----------------|--|
| End point title | Number of subjects reporting any, grade 3 and related unsolicited adverse events (AEs) |
|-----------------|--|

End point description:

Unsolicited AE covers any AE reported in addition to those solicited during the clinical study and any solicited symptom with onset outside the specified period of follow-up for solicited symptoms. Any was defined as occurrence of any unsolicited symptom regardless of intensity grade or relation to vaccination. Grade 3 was an event that prevented normal activities and related was defined as an unsolicited AE assessed by the investigator to be causally related to the study vaccination.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

During the 28-day (Days 0-27) post-vaccination period

| End point values | D-QIV | Control | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 6006 | 6012 | | |
| Units: Subjects | | | | |
| Any unsolicited AEs | 2640 | 2679 | | |
| Grade 3 unsolicited AEs | 160 | 149 | | |
| Related unsolicited AEs | 106 | 116 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any, grade 3 and related AEs with medically attended visits (MAVs)

| | |
|-----------------|---|
| End point title | Number of subjects reporting any, grade 3 and related AEs with medically attended visits (MAVs) |
|-----------------|---|

End point description:

MAVs were defined as AEs with a medically-attended visit i.e. prompting emergency room (ER) visits, hospitalizations or physician visits and that were not routine visits for physical examination or vaccination. Any MAV was defined as at least one MAV experienced. Grade 3 was defined as MAVs that prevented normal activities and related was defined as MAVs assessed by the investigator to be causally related to the study vaccination.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

During the entire study period (approximately 6- 8 months per subject)

| End point values | D-QIV | Control | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 6006 | 6012 | | |
| Units: Subjects | | | | |
| Any MAVs | 3885 | 3988 | | |
| Grade 3 MAVs | 200 | 211 | | |
| Related MAVs | 57 | 58 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any, grade 3 and related potential immune-mediated diseases (pIMDs).

| | |
|-----------------|---|
| End point title | Number of subjects reporting any, grade 3 and related potential immune-mediated diseases (pIMDs). |
|-----------------|---|

End point description:

pIMDs are a subset of adverse events (AEs) that include both clearly autoimmune diseases and also other inflammatory and/or neurologic disorders which may or may not have an autoimmune etiology. Grade 3 = pIMDs that prevented normal activities. Related = symptom assessed by the investigator as causally related to the study vaccination.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

During the entire study period (approximately 6- 8 months per subject)

| End point values | D-QIV | Control | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 6006 | 6012 | | |
| Units: Subjects | | | | |
| Any pIMDs | 5 | 0 | | |
| Grade 3 pIMDs | 3 | 0 | | |
| Related pIMDs | 3 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of subjects reporting any and related serious adverse events (SAEs).

| | |
|-----------------|---|
| End point title | Number of subjects reporting any and related serious adverse events (SAEs). |
|-----------------|---|

End point description:

SAEs assessed include medical occurrences that results in death, are life threatening, require hospitalization or prolongation of hospitalization, results in disability/incapacity or are a congenital anomaly/birth defect in the offspring of a study subjects. Related = symptom assessed by the investigator as causally related to the study vaccination.

| | |
|--|-----------|
| End point type | Secondary |
| End point timeframe: | |
| During the entire study period (approximately 6- 8 months per subject) | |

| End point values | D-QIV | Control | | |
|-----------------------------|-----------------|-----------------|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 6006 | 6012 | | |
| Units: Subjects | | | | |
| Any SAEs | 217 | 201 | | |
| Related SAEs | 6 | 2 | | |
| Fatal SAEs | 1 | 3 | | |
| Related fatal SAEs | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Solicited symptoms were assessed during the 7-day post-vaccination period; unsolicited AEs were assessed during the 28-day post-vaccination period; SAEs were reported during the entire study period (approximately 6- 8 months per subject).

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 19.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------|
| Reporting group title | D-QIV |
|-----------------------|-------|

Reporting group description:

Subjects received 1 or 2 doses of candidate influenza Influsplit™ Tetra vaccine (GSK2321138A).

| | |
|-----------------------|---------|
| Reporting group title | Control |
|-----------------------|---------|

Reporting group description:

In function of their age and D-QIV-vaccine status, subjects received Prevenar 13® or Havrix® Junior and possibly a varicella vaccine (Varilrix® or Varivax/ProVarivax ®).

| Serious adverse events | D-QIV | Control | |
|--|--------------------|--------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 217 / 6006 (3.61%) | 201 / 6012 (3.34%) | |
| number of deaths (all causes) | 1 | 3 | |
| number of deaths resulting from adverse events | | | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Venous thrombosis | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Drowning | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 2 / 6012 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 1 | 0 / 2 | |
| Oedema peripheral | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyrexia | | | |
| subjects affected / exposed | 4 / 6006 (0.07%) | 4 / 6012 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune system disorders | | | |
| Anaphylactic shock | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypersensitivity | | | |
| subjects affected / exposed | 2 / 6006 (0.03%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Reproductive system and breast disorders | | | |
| Balanoposthitis | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Testicular pain | | | |
| subjects affected / exposed | 0 / 6006 (0.00%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Adenoidal hypertrophy | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Apnoea | | | |

| | | | |
|---|------------------|-------------------|--|
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Asthma | | | |
| subjects affected / exposed | 6 / 6006 (0.10%) | 8 / 6012 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 10 | 0 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Asthmatic crisis | | | |
| subjects affected / exposed | 5 / 6006 (0.08%) | 2 / 6012 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 5 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atelectasis | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchial hyperreactivity | | | |
| subjects affected / exposed | 3 / 6006 (0.05%) | 2 / 6012 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchial obstruction | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchospasm | | | |
| subjects affected / exposed | 4 / 6006 (0.07%) | 10 / 6012 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 10 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cough | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dyspnoea | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 6006 (0.02%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pleural effusion | | | |
| subjects affected / exposed | 0 / 6006 (0.00%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Pneumonitis | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wheezing | | | |
| subjects affected / exposed | 3 / 6006 (0.05%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Blood electrolytes abnormal | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Accidental exposure to product | | | |
| subjects affected / exposed | 0 / 6006 (0.00%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Accidental poisoning | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Animal bite | | | |
| subjects affected / exposed | 2 / 6006 (0.03%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|------------------|------------------|--|
| Burns second degree | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 2 / 6012 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chemical poisoning | | | |
| subjects affected / exposed | 0 / 6006 (0.00%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Concussion | | | |
| subjects affected / exposed | 2 / 6006 (0.03%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Foreign body | | | |
| subjects affected / exposed | 0 / 6006 (0.00%) | 2 / 6012 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Foreign body aspiration | | | |
| subjects affected / exposed | 0 / 6006 (0.00%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Head injury | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 2 / 6012 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Laceration | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Near drowning | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pelvic fracture | | | |

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|---|-------------------|-------------------|--|
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Thermal burn | | | |
| subjects affected / exposed | 2 / 6006 (0.03%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wound | | | |
| subjects affected / exposed | 0 / 6006 (0.00%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Congenital, familial and genetic disorders | | | |
| Phimosis | | | |
| subjects affected / exposed | 0 / 6006 (0.00%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Facial paralysis | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Febrile convulsion | | | |
| subjects affected / exposed | 13 / 6006 (0.22%) | 16 / 6012 (0.27%) | |
| occurrences causally related to treatment / all | 2 / 14 | 1 / 16 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Seizure | | | |
| subjects affected / exposed | 3 / 6006 (0.05%) | 2 / 6012 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Seizure anoxic | | | |
| subjects affected / exposed | 0 / 6006 (0.00%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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| Status epilepticus | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 2 / 6006 (0.03%) | 3 / 6012 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypochromic anaemia | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoplastic anaemia | | | |
| subjects affected / exposed | 0 / 6006 (0.00%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Immune thrombocytopenic purpura | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lymphadenitis | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Aphthous ulcer | | | |
| subjects affected / exposed | 0 / 6006 (0.00%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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| Constipation | | | |
| subjects affected / exposed | 0 / 6006 (0.00%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea | | | |
| subjects affected / exposed | 8 / 6006 (0.13%) | 9 / 6012 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 8 | 0 / 9 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastritis | | | |
| subjects affected / exposed | 2 / 6006 (0.03%) | 2 / 6012 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorder | | | |
| subjects affected / exposed | 0 / 6006 (0.00%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ileus | | | |
| subjects affected / exposed | 0 / 6006 (0.00%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Inguinal hernia | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intestinal obstruction | | | |
| subjects affected / exposed | 0 / 6006 (0.00%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Intussusception | | | |

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|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Stomatitis | | | |
| subjects affected / exposed | 3 / 6006 (0.05%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Vomiting | | | |
| subjects affected / exposed | 3 / 6006 (0.05%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Skin and subcutaneous tissue disorders | | | |
| Urticaria | | | |
| subjects affected / exposed | 0 / 6006 (0.00%) | 2 / 6012 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Cystitis haemorrhagic | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nephrotic syndrome | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Abscess | | | |
| subjects affected / exposed | 2 / 6006 (0.03%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abscess limb | | | |
| subjects affected / exposed | 0 / 6006 (0.00%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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|--------------------------|---|------------------|------------------|--|
| Acarodermatitis | subjects affected / exposed | 0 / 6006 (0.00%) | 1 / 6012 (0.02%) | |
| | occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| | deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Amoebiasis | subjects affected / exposed | 3 / 6006 (0.05%) | 3 / 6012 (0.05%) | |
| | occurrences causally related to treatment / all | 0 / 3 | 0 / 3 | |
| | deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Amoebic dysentery | subjects affected / exposed | 8 / 6006 (0.13%) | 3 / 6012 (0.05%) | |
| | occurrences causally related to treatment / all | 0 / 8 | 0 / 3 | |
| | deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Appendicitis | subjects affected / exposed | 0 / 6006 (0.00%) | 1 / 6012 (0.02%) | |
| | occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| | deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Ascariasis | subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| | occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| | deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Atypical pneumonia | subjects affected / exposed | 1 / 6006 (0.02%) | 1 / 6012 (0.02%) | |
| | occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| | deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bacterial infection | subjects affected / exposed | 0 / 6006 (0.00%) | 1 / 6012 (0.02%) | |
| | occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| | deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bacterial pyelonephritis | subjects affected / exposed | 0 / 6006 (0.00%) | 1 / 6012 (0.02%) | |
| | occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| | deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Bronchiolitis | | | | |

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|---|-------------------|-------------------|--|
| subjects affected / exposed | 7 / 6006 (0.12%) | 6 / 6012 (0.10%) | |
| occurrences causally related to treatment / all | 0 / 7 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Bronchitis | | | |
| subjects affected / exposed | 11 / 6006 (0.18%) | 9 / 6012 (0.15%) | |
| occurrences causally related to treatment / all | 0 / 12 | 0 / 9 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chest wall abscess | | | |
| subjects affected / exposed | 0 / 6006 (0.00%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Chikungunya virus infection | | | |
| subjects affected / exposed | 0 / 6006 (0.00%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cholera | | | |
| subjects affected / exposed | 0 / 6006 (0.00%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Conjunctivitis | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Croup infectious | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dengue fever | | | |
| subjects affected / exposed | 2 / 6006 (0.03%) | 10 / 6012 (0.17%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 10 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Diarrhoea infectious | | | |

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|---|-------------------|-------------------|--|
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dysentery | | | |
| subjects affected / exposed | 0 / 6006 (0.00%) | 2 / 6012 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Enterovirus infection | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Escherichia pyelonephritis | | | |
| subjects affected / exposed | 0 / 6006 (0.00%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Escherichia urinary tract infection | | | |
| subjects affected / exposed | 0 / 6006 (0.00%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Exanthema subitum | | | |
| subjects affected / exposed | 0 / 6006 (0.00%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis | | | |
| subjects affected / exposed | 27 / 6006 (0.45%) | 19 / 6012 (0.32%) | |
| occurrences causally related to treatment / all | 0 / 27 | 0 / 20 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis norovirus | | | |
| subjects affected / exposed | 2 / 6006 (0.03%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis rotavirus | | | |

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| subjects affected / exposed | 5 / 6006 (0.08%) | 8 / 6012 (0.13%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 8 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis shigella | | | |
| subjects affected / exposed | 0 / 6006 (0.00%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 4 / 6006 (0.07%) | 2 / 6012 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hand-foot-and-mouth disease | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatitis a | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infection | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infectious mononucleosis | | | |
| subjects affected / exposed | 2 / 6006 (0.03%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Influenza | | | |
| subjects affected / exposed | 0 / 6006 (0.00%) | 2 / 6012 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Laryngitis | | | |

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|---|------------------|------------------|--|
| subjects affected / exposed | 4 / 6006 (0.07%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 6 / 6006 (0.10%) | 3 / 6012 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 6 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mastoiditis | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Meningitis viral | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Mycoplasma infection | | | |
| subjects affected / exposed | 0 / 6006 (0.00%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 2 / 6006 (0.03%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Otitis media | | | |
| subjects affected / exposed | 4 / 6006 (0.07%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Otitis media acute | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 2 / 6012 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Parasitic gastroenteritis | | | |

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|---|-------------------|-------------------|--|
| subjects affected / exposed | 0 / 6006 (0.00%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Periorbital cellulitis | | | |
| subjects affected / exposed | 3 / 6006 (0.05%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 3 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Peritonsillar abscess | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pharyngitis | | | |
| subjects affected / exposed | 2 / 6006 (0.03%) | 5 / 6012 (0.08%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 5 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pharyngotonsillitis | | | |
| subjects affected / exposed | 0 / 6006 (0.00%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 56 / 6006 (0.93%) | 66 / 6012 (1.10%) | |
| occurrences causally related to treatment / all | 0 / 60 | 0 / 71 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 0 / 6006 (0.00%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia measles | | | |
| subjects affected / exposed | 0 / 6006 (0.00%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia mycoplasmal | | | |

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|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 6006 (0.00%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia respiratory syncytial viral | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia viral | | | |
| subjects affected / exposed | 2 / 6006 (0.03%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pyelonephritis | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory syncytial virus bronchiolitis | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 0 / 6006 (0.00%) | 2 / 6012 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rotavirus infection | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sepsis | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sinusitis | | | |

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|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tonsillitis | | | |
| subjects affected / exposed | 2 / 6006 (0.03%) | 2 / 6012 (0.03%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Tuberculosis | | | |
| subjects affected / exposed | 0 / 6006 (0.00%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Typhoid fever | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 3 / 6012 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 4 / 6006 (0.07%) | 3 / 6012 (0.05%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 3 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 4 / 6006 (0.07%) | 4 / 6012 (0.07%) | |
| occurrences causally related to treatment / all | 0 / 4 | 0 / 4 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Varicella | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral infection | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral rash | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 0 / 6006 (0.00%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral rhinitis | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Viral sepsis | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Wound infection | | | |
| subjects affected / exposed | 0 / 6006 (0.00%) | 1 / 6012 (0.02%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 8 / 6006 (0.13%) | 7 / 6012 (0.12%) | |
| occurrences causally related to treatment / all | 0 / 9 | 0 / 7 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypoglycaemia | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hypokalaemia | | | |
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Malnutrition | | | |
| subjects affected / exposed | 2 / 6006 (0.03%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Polydipsia | | | |

| | | | |
|---|------------------|------------------|--|
| subjects affected / exposed | 1 / 6006 (0.02%) | 0 / 6012 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | D-QIV | Control | |
|---|----------------------|----------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 3427 / 6006 (57.06%) | 3501 / 6012 (58.23%) | |
| Nervous system disorders | | | |
| Somnolence | | | |
| subjects affected / exposed | 1025 / 6006 (17.07%) | 1129 / 6012 (18.78%) | |
| occurrences (all) | 1259 | 1388 | |
| General disorders and administration site conditions | | | |
| Pain | | | |
| subjects affected / exposed | 1351 / 6006 (22.49%) | 1376 / 6012 (22.89%) | |
| occurrences (all) | 1824 | 1868 | |
| Pyrexia | | | |
| subjects affected / exposed | 866 / 6006 (14.42%) | 949 / 6012 (15.79%) | |
| occurrences (all) | 954 | 1042 | |
| Swelling | | | |
| subjects affected / exposed | 665 / 6006 (11.07%) | 743 / 6012 (12.36%) | |
| occurrences (all) | 842 | 928 | |
| Skin and subcutaneous tissue disorders | | | |
| Erythema | | | |
| subjects affected / exposed | 983 / 6006 (16.37%) | 1094 / 6012 (18.20%) | |
| occurrences (all) | 1365 | 1467 | |
| Psychiatric disorders | | | |
| Irritability | | | |
| subjects affected / exposed | 1385 / 6006 (23.06%) | 1428 / 6012 (23.75%) | |
| occurrences (all) | 1734 | 1808 | |
| Infections and infestations | | | |
| Nasopharyngitis | | | |

| | | | |
|------------------------------------|-------------------------|-------------------------|--|
| subjects affected / exposed | 871 / 6006 (14.50%) | 943 / 6012 (15.69%) | |
| occurrences (all) | 1050 | 1111 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 522 / 6006 (8.69%) | 516 / 6012 (8.58%) | |
| occurrences (all) | 629 | 609 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 1230 / 6006 (20.48%) | 1293 / 6012 (21.51%) | |
| occurrences (all) | 1504 | 1561 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported