# Clinical trial results:
# A randomised, controlled, multidose, multicentre, adaptive phase II/III study in infants with proliferating infantile hemangiomas requiring systemic therapy to compare four regimens of propranolol (1 or 3 mg/kg/day for 3 or 6 months) to placebo (double blind).

## Summary

| | |
|---|---|
| EudraCT number | 2009-013262-84 |
| Trial protocol | FR DE ES IT HU LT CZ RO |
| Global end of trial date | 05 November 2013 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 17 February 2016 |
| First version publication date | 17 February 2016 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | V00400SB201 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01056341 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Pierre Fabre Dermatologie |
| Sponsor organisation address | 45, Place Abel Gance, Boulogne, France, 92100 |
| Public contact | Medical and/or Clinical Study Manager, Pierre Fabre Dermatologie, contact_essais_cliniques@pierre-fabre.com |
| Scientific contact | Medical and/or Clinical Study Manager, Pierre Fabre Dermatologie, contact_essais_cliniques@pierre-fabre.com |

Notes:

**Paediatric regulatory details**

| | |
|---|---|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMEA-000511-PIP01-08 |
| 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? | No |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 05 May 2014 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 08 May 2012 |
| Global end of trial reached? | Yes |
| Global end of trial date | 05 November 2013 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To identify the appropriate dose and duration of propranolol treatment (as coded V0400SB) out of four regimens of oral propranolol (1 or 3 mg/kg/day twice a day for 3 or 6 months), and to demonstrate its superiority over placebo based on the complete/nearly complete resolution of the target IH at Week 24.

Protection of trial subjects:

Clinical (including respiratory rate and vital sign measurements) and paraclinical (lab tests (haematology, biochemistry, glycaemia (pin-prick), and ECG) examinations.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 24 February 2010 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety, Efficacy |
| Long term follow-up duration | 17 Months |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Poland: 26 |
| Country: Number of subjects enrolled | Romania: 7 |
| Country: Number of subjects enrolled | Spain: 59 |
| Country: Number of subjects enrolled | Czech Republic: 8 |
| Country: Number of subjects enrolled | France: 114 |
| Country: Number of subjects enrolled | Germany: 60 |
| Country: Number of subjects enrolled | Hungary: 11 |
| Country: Number of subjects enrolled | Italy: 2 |
| Country: Number of subjects enrolled | Lithuania: 18 |
| Country: Number of subjects enrolled | United States: 53 |
| Country: Number of subjects enrolled | Russian Federation: 3 |
| Country: Number of subjects enrolled | Mexico: 5 |
| Country: Number of subjects enrolled | Canada: 18 |
| Country: Number of subjects enrolled | Peru: 35 |
| Country: Number of subjects enrolled | Australia: 32 |
| Country: Number of subjects enrolled | New Zealand: 5 |
| Worldwide total number of subjects | 456 |
| EEA total number of subjects | 305 |

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) | 456 |
| 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:

510 patients were included in the study (Informed Consent Form signed). Among these 510 patients, 50 were screen failure, 460 were randomized and 456 were randomized and treated.

### Pre-assignment

Screening details:

Infants 1 to 5 months of age with proliferating infantile hemangioma requiring systemic therapy. Infants were randomly assigned to receive placebo or one of four propranolol regimens (1 or 3 mg of propranolol base per kilogram of body weight per day for 3 or 6 months).

### Period 1

| | |
|---|---|
| Period 1 title | 24-week study treatment period |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Investigator, Monitor, Data analyst, Carer, Subject, Assessor |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Placebo |

Arm description: -

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

Dosage and administration details:

Treatment with placebo for 6 months twice daily.

| | |
|---|---|
| **Arm title** | Propranolol 1mg/kg/day - 3 months |

Arm description: -

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Propranolol hydrochloride oral solution |
| Investigational medicinal product code | V0400SB |
| Other name | Hemangiol |
| Pharmaceutical forms | Oral solution |
| Routes of administration | Oral use |

Dosage and administration details:

Propranolol hydrochloride oral solution 1mg/kg/day for 3 months, then placebo for 3 months.

| | |
|---|---|
| **Arm title** | Propranolol 1mg/kg/day - 6 months |

Arm description: -

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Propranolol hydrochloride oral solution |
| Investigational medicinal product code | V0400SB |
| Other name | Hemangiol |
| Pharmaceutical forms | Oral solution |
| Routes of administration | Oral use |

Dosage and administration details:

Propranolol  hydrochloride oral solution 1mg/kg/day for 6 months.

| **Arm title** | Propranolol 3 mg/kg/day - 3 months |
|---|---|
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | Propranolol hydrochloride oral solution |
| Investigational medicinal product code | V0400SB |
| Other name | Hemangiol |
| Pharmaceutical forms | Oral solution |
| Routes of administration | Oral use |

Dosage and administration details:

Propranolol hydrochloride oral solution 3 mg/kg/day for 3 months, then placebo for 3 months.

| **Arm title** | Propranolol 3 mg/kg/day - 6 months |
|---|---|
| Arm description: - | |
| Arm type | Experimental |
| Investigational medicinal product name | Propranolol hydrochloride oral solution |
| Investigational medicinal product code | V0400SB |
| Other name | Hemangiol |
| Pharmaceutical forms | Oral solution |
| Routes of administration | Oral use |

Dosage and administration details:

Propranolol hydrochloride oral solution 3mg/kg/day for 6 months.

| **Number of subjects in period 1** | Placebo | Propranolol 1mg/kg/day - 3 months | Propranolol 1mg/kg/day - 6 months |
|---|---|---|---|
| Started | 55 | 98 | 102 |
| Interim analysis | 25 | 41 [1] | 40 [2] |
| Completed | 19 | 63 | 88 |
| Not completed | 36 | 35 | 14 |
| Consent withdrawn by subject | 3 | 1 | 4 |
| Physician decision | - | - | - |
| Treatment intolerance | - | 2 | - |
| Adverse event, non-fatal | - | - | 1 |
| Moving of parents | - | 1 | - |
| Lost to follow-up | 1 | 1 | 2 |
| Lack of efficacy | 32 | 30 | 7 |

| **Number of subjects in period 1** | Propranolol 3 mg/kg/day - 3 months | Propranolol 3 mg/kg/day - 6 months |
|---|---|---|
| Started | 100 | 101 |
| Interim analysis | 39 [3] | 43 [4] |
| Completed | 65 | 88 |
| Not completed | 35 | 13 |
| Consent withdrawn by subject | 3 | 2 |
| Physician decision | 1 | - |

| | | |
|---|---|---|
| Treatment intolerance | - | - |
| Adverse event, non-fatal | 4 | 1 |
| Moving of parents | 2 | - |
| Lost to follow-up | - | 1 |
| Lack of efficacy | 25 | 9 |

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: A planned interim analysis was conducted to identify the regimen to study for the final efficacy analysis.

At this milestone, all patients were not included in the arm (41/98). During this analysis, the recruitment was not interrupted.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: A planned interim analysis was conducted to identify the regimen to study for the final efficacy analysis.

At this milestone, all patients were not included in the arm (40/102). During this analysis, the recruitment was not interrupted.

[3] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: A planned interim analysis was conducted to identify the regimen to study for the final efficacy analysis.

At this milestone, all patients were not included in the arm (30/100). During this analysis, the recruitment was not interrupted.

[4] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: A planned interim analysis was conducted to identify the regimen to study for the final efficacy analysis.

At this milestone, all patients were not included in the arm (43/101). During this analysis, the recruitment was not interrupted.

## Period 2

| | |
|---|---|
| Period 2 title | 72-week follow-up period (no study drug) |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst, Carer, Assessor |

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Placebo |
| Arm description: - | |
| Arm type | No intervention |
| No investigational medicinal product assigned in this arm | |
| **Arm title** | Propranolol 1mg/kg/day - 3 months |
| Arm description: - | |
| Arm type | No intervention |
| No investigational medicinal product assigned in this arm | |
| **Arm title** | Propranolol 1mg/kg/day - 6 months |
| Arm description: - | |
| Arm type | No intervention |
| No investigational medicinal product assigned in this arm | |

| **Arm title** | Propranolol 3 mg/kg/day - 3 months |
|---|---|
| Arm description: - | |
| Arm type | No intervention |
| No investigational medicinal product assigned in this arm | |

| **Arm title** | Propranolol 3 mg/kg/day - 6 months |
|---|---|
| Arm description: - | |
| Arm type | No intervention |
| No investigational medicinal product assigned in this arm | |

| **Number of subjects in period 2[5]** | Placebo | Propranolol 1mg/kg/day - 3 months | Propranolol 1mg/kg/day - 6 months |
|---|---|---|---|
| Started | 19 | 60 | 85 |
| Completed | 28 | 75 | 82 |
| Not completed | 5 | 10 | 9 |
| Physician decision | - | - | 1 |
| Patient's Parent(s) or guardian(s) decision | 3 | 5 | 4 |
| Visit schedule not respected | - | - | 2 |
| Lost to follow-up | 2 | 4 | 2 |
| off-label medication started | - | - | - |
| Patient moved to another city | - | 1 | - |
| Joined | 14 | 25 | 6 |
| prematurely discontinued the treatment period | 14 | 25 | 6 |

| **Number of subjects in period 2[5]** | Propranolol 3 mg/kg/day - 3 months | Propranolol 3 mg/kg/day - 6 months |
|---|---|---|
| Started | 65 | 87 |
| Completed | 78 | 80 |
| Not completed | 9 | 15 |
| Physician decision | - | 1 |
| Patient's Parent(s) or guardian(s) decision | 7 | 7 |
| Visit schedule not respected | - | - |
| Lost to follow-up | 2 | 6 |
| off-label medication started | - | 1 |
| Patient moved to another city | - | - |
| Joined | 22 | 8 |
| prematurely discontinued the treatment period | 22 | 8 |

Notes:

[5] - 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: 7 patients discontinued study after the end of treatment period, and patients prematurely discontinued the treatment period could also entered the follow period.
-Placebo group : 33 patients entered the follow-up period(FU), 19 completed(C) + 14 prematurely discontinued(PDO) for the treatment period
- 1mg/kg/day-3months group: 85 FU= 60(C)+25(PDO)
- 1mg/kg/day-6months group: 91 FU=85(C)+6(PDO)
- 3mg/kg/day-3months group, 87 FU=65(C)+22(PDO)
- 3mg/kg/day-6months group, 95 FU= 87(C)+8(PDO)

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Placebo |
| Reporting group description: - | |
| Reporting group title | Propranolol 1mg/kg/day - 3 months |
| Reporting group description: - | |
| Reporting group title | Propranolol 1mg/kg/day - 6 months |
| Reporting group description: - | |
| Reporting group title | Propranolol 3 mg/kg/day - 3 months |
| Reporting group description: - | |
| Reporting group title | Propranolol 3 mg/kg/day - 6 months |
| Reporting group description: - | |

| Reporting group values | Placebo | Propranolol 1mg/kg/day - 3 months | Propranolol 1mg/kg/day - 6 months |
|---|---|---|---|
| Number of subjects | 55 | 98 | 102 |
| Age categorical<br>Units: Subjects | | | |
| Age continuous<br>Units: days | | | |
| arithmetic mean | 103.91 | 103.58 | 102.65 |
| standard deviation | ± 31.06 | ± 33.07 | ± 30.12 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 38 | 68 | 70 |
| Male | 17 | 30 | 32 |

| Reporting group values | Propranolol 3 mg/kg/day - 3 months | Propranolol 3 mg/kg/day - 6 months | Total |
|---|---|---|---|
| Number of subjects | 100 | 101 | 456 |
| Age categorical<br>Units: Subjects | | | |
| Age continuous<br>Units: days | | | |
| arithmetic mean | 107.53 | 101.63 | |
| standard deviation | ± 30.14 | ± 31 | - |
| Gender categorical<br>Units: Subjects | | | |
| Female | 79 | 70 | 325 |
| Male | 21 | 31 | 131 |

| Subject analysis sets | |
|---|---|
| Subject analysis set title | 24-week treatment safety analysis data set |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Patients randomized and treated.

| Subject analysis set title | 72-week follow-up safety analysis data set |
|---|---|
| Subject analysis set type | Safety analysis |

Subject analysis set description:

Among the 456 patients randomized and treated, 391 entered the 72-week follow-up period.

| **Reporting group values** | 24-week treatment safety analysis data set | 72-week follow-up safety analysis data set | |
|---|---|---|---|
| Number of subjects | 456 | 391 | |
| Age categorical<br>Units: Subjects | | | |
| Age continuous<br>Units: days<br>arithmetic mean<br>standard deviation | <br><br>103.85<br>± 31.02 | <br><br><br>± | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 325 | | |
| Male | 131 | | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Placebo |
| Reporting group description: - | |
| Reporting group title | Propranolol 1mg/kg/day - 3 months |
| Reporting group description: - | |
| Reporting group title | Propranolol 1mg/kg/day - 6 months |
| Reporting group description: - | |
| Reporting group title | Propranolol 3 mg/kg/day - 3 months |
| Reporting group description: - | |
| Reporting group title | Propranolol 3 mg/kg/day - 6 months |
| Reporting group description: - | |
| Reporting group title | Placebo |
| Reporting group description: - | |
| Reporting group title | Propranolol 1mg/kg/day - 3 months |
| Reporting group description: - | |
| Reporting group title | Propranolol 1mg/kg/day - 6 months |
| Reporting group description: - | |
| Reporting group title | Propranolol 3 mg/kg/day - 3 months |
| Reporting group description: - | |
| Reporting group title | Propranolol 3 mg/kg/day - 6 months |
| Reporting group description: - | |
| Subject analysis set title | 24-week treatment safety analysis data set |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| Patients randomized and treated. | |
| Subject analysis set title | 72-week follow-up safety analysis data set |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| Among the 456 patients randomized and treated, 391 entered the 72-week follow-up period. | |

### Primary: Interim analysis - Complete/nearly complete resolution of target IH at Week 24

| | |
|---|---|
| End point title | Interim analysis - Complete/nearly complete resolution of target IH at Week 24 |

End point description:

Percentage of patients with complete/nearly complete resolution (CR/NCR) of target IH at week 24 (based on Intra-patient Blinded Centralized Independent Qualitative Assessments of Photographs at week 24 compared to baseline) in the interim efficacy analysis set (n=188 patients having completed their week 24 or been withdrawn prematurely from treatment period).

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

End point timeframe:

Week 24 (endpoint)

| End point values | Placebo | Propranolol 1mg/kg/day - 3 months | Propranolol 1mg/kg/day - 6 months | Propranolol 3 mg/kg/day - 3 months |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 25 | 41 | 40 | 39 |
| Units: percentage of patients | | | | |
| number (not applicable) | 8 | 9.8 | 37.5 | 7.7 |

| End point values | Propranolol 3 mg/kg/day - 6 months | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 43 | | | |
| Units: percentage of patients | | | | |
| number (not applicable) | 62.8 | | | |

**Statistical analyses**

| Statistical analysis title | Interim analysis Target IH CR/NCR at Week24 |
|---|---|
| Comparison groups | Placebo v Propranolol 1mg/kg/day - 3 months v Propranolol 1mg/kg/day - 6 months v Propranolol 3 mg/kg/day - 3 months v Propranolol 3 mg/kg/day - 6 months |
| Number of subjects included in analysis | 188 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | One-sided Z-tests |

**Primary: Primary analysis - Success on target IH evolution at Week 24**

| End point title | Primary analysis - Success on target IH evolution at Week 24[1] |
|---|---|

End point description:

Percentage of patients with success at week 24 = Percentage of patients with CR/NCR of target IH at week 24 (based on the intra-patient blinded centralized independent qualitative assessments of photographs of the target IH at week 24 compared to baseline) with no additional criteria of failure (early treatment withdrawal, use of prohibited treatment, no centralized or investigator's assessment of target IH evolution at week 24) in the ITT set (n=276). The final comparison is performed between the ITT placebo and propranolol 3 mg/kg/day - 6 months groups (n=156).

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

End point timeframe:

Week 24

Notes:

[1] - 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: On the basis of an interim analysis of the first 188 patients who completed 24 weeks of trial treatment, the regimen of 3 mg of propranolol per kilogram per day for 6 months was selected for the final efficacy analysis.
The primary analysis of the primary endpoint compared only the selected regimen (3mg/kg/day-6months) to placebo. No statistical comparaison on the other arms to placebo were performed at Week 24.

| End point values | Placebo | Propranolol 3 mg/kg/day - 6 months | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 55 | 101 | | |
| Units: percentage of patients | | | | |
| number (not applicable) | 3.6 | 60.4 | | |

## Statistical analyses

| Statistical analysis title | W24 primary analysis - Primary efficacy endpoint |
|---|---|

Statistical analysis description:

Posch et al method for an adaptive confirmatory design with a single selection at an interim analysis with a type I error level maintained at 0.005

| | |
|---|---|
| Comparison groups | Placebo v Propranolol 3 mg/kg/day - 6 months |
| Number of subjects included in analysis | 156 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | < 0.0001 |
| Method | Posh et al method,type I error at 0.005 |

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: During the whole study period. | |
| Assessment type | Non-systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 13.1 |

| Reporting groups | |
|---|---|
| Reporting group title | W24-treatment period-safety set- Placebo |
| Reporting group description: - | |
| Reporting group title | W24-treatment period-safety set-1mg/kg/D,3months |
| Reporting group description: - | |
| Reporting group title | W24-treatment period-safety set-1mg/kg/D,6months |
| Reporting group description: - | |
| Reporting group title | W24-treatment period-safety set-3mg/kg/D,3months |
| Reporting group description: - | |
| Reporting group title | W24-treatment period-safety set-3mg/kg/D,6months |
| Reporting group description: - | |
| Reporting group title | W72-follow-up period of placebo group-safety set |
| Reporting group description: - | |
| Reporting group title | W72-follow-up period of 1mg/kg/D,3months group-safety set |
| Reporting group description: - | |
| Reporting group title | W72-follow-up period of 1mg/kg/D,6months group-safety set |
| Reporting group description: - | |
| Reporting group title | W72-follow-up period of 3mg/kg/D,3months group-safety set |
| Reporting group description: - | |
| Reporting group title | W72-follow-up period of 3mg/kg/D,6months group-safety set |
| Reporting group description: - | |

| Serious adverse events | W24-treatment period-safety set-Placebo | W24-treatment period-safety set-1mg/kg/D,3months | W24-treatment period-safety set-1mg/kg/D,6months |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 3 / 55 (5.45%) | 5 / 98 (5.10%) | 3 / 102 (2.94%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Traumatic brain injury | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (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 | | | |
| Hip dysplasia | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (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 |
| Cardiac disorders | | | |
| Atrioventricular block second degree | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 1 / 98 (1.02%) | 0 / 102 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bradycardia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (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 |
| Cyanosis | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (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 |
| Surgical and medical procedures | | | |
| Cataract operation | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 1 / 98 (1.02%) | 0 / 102 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ileostomy closure | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 1 / 102 (0.98%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Inguinal hernia repair | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 1 / 102 (0.98%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Surgery | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (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 |
| Finger amputation | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (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 |
| Hip surgery | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (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 |
| Hospitalisation | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (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 |
| Scrotal operation | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (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 |
| Nervous system disorders | | | |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 1 / 102 (0.98%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Convulsion | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (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 |
| Febrile convulsion | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (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 |
| General disorders and administration site conditions | | | |

| | | | |
|---|---|---|---|
| Drug ineffective | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 1 / 98 (1.02%) | 0 / 102 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Condition aggravated | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 2 / 55 (3.64%) | 0 / 98 (0.00%) | 0 / 102 (0.00%) |
| occurrences causally related to treatment / all | 1 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Inflammation | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (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 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (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 |
| Hyperthermia | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (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 | | | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (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 |
| Enterocolitis | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (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, thoracic and mediastinal disorders | | | |
| Asphyxia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (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 |
| Asthma | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (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 |
| Cough | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (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 |
| Psychiatric disorders | | | |
| Apathy | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (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 |
| Infections and infestations | | | |
| Bronchiolitis | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 1 / 98 (1.02%) | 0 / 102 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (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 |
| Bronchopneumonia | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 1 / 102 (0.98%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cystitis | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 1 / 98 (1.02%) | 0 / 102 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 1 / 102 (0.98%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (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 |
| Rotavirus infection | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (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 |
| Viraemia | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (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 tract infection viral | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (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 |
| Ear infection | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (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 |
| Gastroenteritis rotavirus | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (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 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (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 |
| Otitis media acute | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (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 syncytial virus infection | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (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 |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (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 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (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 | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (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 |
| Ketoacidosis | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (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 |
| Type 1 diabetes mellitus | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (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 |

| **Serious adverse events** | W24-treatment period-safety set-3mg/kg/D,3months | W24-treatment period-safety set-3mg/kg/D,6months | W72-follow-up period of placebo group-safety set |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 9 / 100 (9.00%) | 6 / 101 (5.94%) | 5 / 33 (15.15%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from | 0 | 0 | 0 |

| adverse events | | | |
|---|---|---|---|
| Injury, poisoning and procedural complications | | | |
| Traumatic brain injury | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 1 / 101 (0.99%) | 0 / 33 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Congenital, familial and genetic disorders | | | |
| Hip dysplasia | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 0 / 33 (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 |
| Cardiac disorders | | | |
| Atrioventricular block second degree | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 0 / 33 (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 |
| Bradycardia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 0 / 101 (0.00%) | 0 / 33 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cyanosis | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 0 / 101 (0.00%) | 0 / 33 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Surgical and medical procedures | | | |
| Cataract operation | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 0 / 33 (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 |
| Ileostomy closure | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 0 / 33 (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 |
| Inguinal hernia repair | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 0 / 33 (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 |
| Surgery | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 0 / 33 (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 |
| Finger amputation | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 0 / 33 (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 |
| Hip surgery | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 0 / 33 (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 |
| Hospitalisation | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 0 / 33 (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 |
| Scrotal operation | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 1 / 33 (3.03%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 0 / 33 (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 |
| Convulsion | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 0 / 33 (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 |
| Febrile convulsion | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 0 / 33 (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 |
| General disorders and administration site conditions | | | |
| Drug ineffective | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 1 / 101 (0.99%) | 0 / 33 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Condition aggravated | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 0 / 101 (0.00%) | 0 / 33 (0.00%) |
| occurrences causally related to treatment / all | 1 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Inflammation | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 0 / 33 (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 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 0 / 33 (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 |
| Hyperthermia | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 0 / 33 (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 | | | |
| Gastrooesophageal reflux disease | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 100 (2.00%) | 0 / 101 (0.00%) | 0 / 33 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Enterocolitis | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 0 / 101 (0.00%) | 0 / 33 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asphyxia | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 0 / 33 (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 |
| Asthma | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 0 / 33 (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 |
| Cough | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 0 / 33 (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 |
| Psychiatric disorders | | | |
| Apathy | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 1 / 101 (0.99%) | 0 / 33 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Bronchiolitis | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 1 / 101 (0.99%) | 1 / 33 (3.03%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 1 / 101 (0.99%) | 1 / 33 (3.03%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|---|---|---|
| Bronchopneumonia | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 0 / 33 (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 |
| Cystitis | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 0 / 33 (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 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 1 / 33 (3.03%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 3 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pyelonephritis | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 0 / 101 (0.00%) | 0 / 33 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Rotavirus infection | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 0 / 101 (0.00%) | 0 / 33 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viraemia | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 0 / 101 (0.00%) | 0 / 33 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory tract infection viral | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 0 / 33 (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 |
| Ear infection | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 0 / 33 (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 |
| Gastroenteritis rotavirus | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 0 / 33 (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 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 0 / 33 (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 |
| Otitis media acute | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 1 / 33 (3.03%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory syncytial virus infection | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 1 / 33 (3.03%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 0 / 33 (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 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 0 / 33 (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 | 1 / 100 (1.00%) | 0 / 101 (0.00%) | 0 / 33 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ketoacidosis | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 0 / 33 (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 |
| Type 1 diabetes mellitus | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 0 / 33 (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 |

| **Serious adverse events** | W72-follow-up period of 1mg/kg/D,3months group-safety set | W72-follow-up period of 1mg/kg/D,6months group-safety set | W72-follow-up period of 3mg/kg/D,3months group-safety set |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 6 / 85 (7.06%) | 5 / 91 (5.49%) | 5 / 87 (5.75%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Traumatic brain injury | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 0 / 87 (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 | | | |
| Hip dysplasia | | | |
| subjects affected / exposed | 1 / 85 (1.18%) | 0 / 91 (0.00%) | 0 / 87 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Atrioventricular block second degree | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 0 / 87 (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 |
| Bradycardia | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 0 / 87 (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 |
| Cyanosis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 0 / 87 (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 |
| Surgical and medical procedures | | | |
| Cataract operation | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 0 / 87 (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 |
| Ileostomy closure | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 0 / 87 (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 |
| Inguinal hernia repair | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 0 / 87 (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 |
| Surgery | | | |
| subjects affected / exposed | 1 / 85 (1.18%) | 0 / 91 (0.00%) | 0 / 87 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Finger amputation | | | |
| subjects affected / exposed | 1 / 85 (1.18%) | 0 / 91 (0.00%) | 0 / 87 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hip surgery | | | |
| subjects affected / exposed | 1 / 85 (1.18%) | 0 / 91 (0.00%) | 0 / 87 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hospitalisation | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 1 / 87 (1.15%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Scrotal operation | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 0 / 87 (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 |
| Nervous system disorders | | | |
| Epilepsy | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 0 / 87 (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 |
| Convulsion | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 1 / 87 (1.15%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Febrile convulsion | | | |
| subjects affected / exposed | 1 / 85 (1.18%) | 0 / 91 (0.00%) | 0 / 87 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Drug ineffective | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 0 / 87 (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 |
| Condition aggravated | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 0 / 87 (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 |
| Inflammation | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 0 / 87 (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 |
| Pyrexia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 0 / 87 (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 |
| Hyperthermia | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 1 / 87 (1.15%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 0 / 87 (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 |
| Enterocolitis | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 0 / 87 (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, thoracic and mediastinal disorders | | | |
| Asphyxia | | | |
| subjects affected / exposed | 1 / 85 (1.18%) | 0 / 91 (0.00%) | 0 / 87 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Asthma | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 1 / 91 (1.10%) | 0 / 87 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cough | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 1 / 87 (1.15%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Apathy | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 0 / 87 (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 |

| | | | |
|---|---|---|---|
| Infections and infestations | | | |
| Bronchiolitis | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 1 / 87 (1.15%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 85 (1.18%) | 0 / 91 (0.00%) | 0 / 87 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchopneumonia | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 0 / 87 (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 |
| Cystitis | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 0 / 87 (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 |
| Gastroenteritis | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 0 / 87 (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 |
| Pyelonephritis | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 0 / 87 (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 |
| Rotavirus infection | | | |
| subjects affected / exposed | 1 / 85 (1.18%) | 0 / 91 (0.00%) | 2 / 87 (2.30%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 2 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viraemia | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 0 / 87 (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 tract infection viral | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 0 / 87 (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 |
| Ear infection | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 1 / 87 (1.15%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastroenteritis rotavirus | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 1 / 91 (1.10%) | 0 / 87 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 1 / 87 (1.15%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Otitis media acute | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 0 / 87 (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 syncytial virus infection | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 0 / 87 (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 |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 1 / 91 (1.10%) | 0 / 87 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |
| subjects affected / exposed | 2 / 85 (2.35%) | 0 / 91 (0.00%) | 0 / 87 (0.00%) |
| occurrences causally related to treatment / all | 0 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 85 (0.00%) | 1 / 91 (1.10%) | 0 / 87 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Ketoacidosis | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 1 / 91 (1.10%) | 0 / 87 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Type 1 diabetes mellitus | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 1 / 91 (1.10%) | 0 / 87 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| **Serious adverse events** | W72-follow-up period of 3mg/kg/D,6months group-safety set | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 7 / 95 (7.37%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Injury, poisoning and procedural complications | | | |
| Traumatic brain injury | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Congenital, familial and genetic disorders | | | |
| Hip dysplasia | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Atrioventricular block second degree | | | |
| alternative assessment type: Systematic | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|---|---|---|---|---|
| Bradycardia | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cyanosis | | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Surgical and medical procedures | | | | |
| Cataract operation | | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ileostomy closure | | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Inguinal hernia repair | | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Surgery | | | | |
| subjects affected / exposed | 1 / 95 (1.05%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Finger amputation | | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hip surgery | | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |

| | | | | |
|---|---|---|---|---|
| Hospitalisation | | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Scrotal operation | | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Nervous system disorders | | | | |
| Epilepsy | | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Convulsion | | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Febrile convulsion | | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| General disorders and administration site conditions | | | | |
| Drug ineffective | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Condition aggravated | | | | |
| alternative assessment type: Systematic | | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Inflammation | | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 1 / 95 (1.05%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pyrexia | | | | |
| subjects affected / exposed | 1 / 95 (1.05%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Hyperthermia | | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastrointestinal disorders | | | | |
| Gastrooesophageal reflux disease | | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Enterocolitis | | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Respiratory, thoracic and mediastinal disorders | | | | |
| Asphyxia | | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Asthma | | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Cough | | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |

| | | | |
|---|---|---|---|
| Psychiatric disorders | | | |
| Apathy | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Bronchiolitis | | | |
| subjects affected / exposed | 2 / 95 (2.11%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bronchopneumonia | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cystitis | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 1 / 95 (1.05%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pyelonephritis | | | |
| subjects affected / exposed | 1 / 95 (1.05%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Rotavirus infection | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | | |
|---|---|---|---|---|
| Viraemia | | | | |
| subjects affected / exposed | 0 / 95 (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 | 1 / 95 (1.05%) | | | |
| occurrences causally related to treatment / all | 0 / 1 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Ear infection | | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Gastroenteritis rotavirus | | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Nasopharyngitis | | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Otitis media acute | | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Respiratory syncytial virus infection | | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Tonsillitis | | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | | |
| occurrences causally related to treatment / all | 0 / 0 | | | |
| deaths causally related to treatment / all | 0 / 0 | | | |
| Pneumonia | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 95 (1.05%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ketoacidosis | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Type 1 diabetes mellitus | | | |
| subjects affected / exposed | 0 / 95 (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** | W24-treatment period-safety set-Placebo | W24-treatment period-safety set-1mg/kg/D,3months | W24-treatment period-safety set-1mg/kg/D,6months |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 40 / 55 (72.73%) | 88 / 98 (89.80%) | 92 / 102 (90.20%) |
| Injury, poisoning and procedural complications | | | |
| Vaccination complication | | | |
| subjects affected / exposed | 2 / 55 (3.64%) | 7 / 98 (7.14%) | 9 / 102 (8.82%) |
| occurrences (all) | 2 | 7 | 12 |
| Vascular disorders | | | |
| Peripheral coldness | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 8 / 98 (8.16%) | 10 / 102 (9.80%) |
| occurrences (all) | 1 | 9 | 12 |
| Nervous system disorders | | | |
| Somnolence | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 6 / 98 (6.12%) | 4 / 102 (3.92%) |
| occurrences (all) | 1 | 13 | 5 |
| Hypotonia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 55 (0.00%) | 1 / 98 (1.02%) | 1 / 102 (0.98%) |
| occurrences (all) | 0 | 1 | 1 |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 6 / 55 (10.91%) | 21 / 98 (21.43%) | 24 / 102 (23.53%) |
| occurrences (all) | 6 | 32 | 40 |
| Irritability | | | |
| subjects affected / exposed | 3 / 55 (5.45%) | 5 / 98 (5.10%) | 6 / 102 (5.88%) |
| occurrences (all) | 3 | 7 | 6 |
| Condition aggravated | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 3 / 98 (3.06%) | 1 / 102 (0.98%) |
| occurrences (all) | 0 | 4 | 2 |
| Eye disorders | | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 2 / 55 (3.64%) | 4 / 98 (4.08%) | 8 / 102 (7.84%) |
| occurrences (all) | 3 | 6 | 9 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 4 / 55 (7.27%) | 16 / 98 (16.33%) | 14 / 102 (13.73%) |
| occurrences (all) | 9 | 26 | 17 |
| Teething | | | |
| subjects affected / exposed | 6 / 55 (10.91%) | 19 / 98 (19.39%) | 23 / 102 (22.55%) |
| occurrences (all) | 7 | 25 | 45 |
| Vomiting | | | |
| subjects affected / exposed | 3 / 55 (5.45%) | 16 / 98 (16.33%) | 13 / 102 (12.75%) |
| occurrences (all) | 7 | 24 | 16 |
| Toothache | | | |
| subjects affected / exposed | 2 / 55 (3.64%) | 5 / 98 (5.10%) | 2 / 102 (1.96%) |
| occurrences (all) | 2 | 6 | 3 |
| Constipation | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 9 / 98 (9.18%) | 6 / 102 (5.88%) |
| occurrences (all) | 3 | 15 | 9 |
| Gingival pain | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 3 / 98 (3.06%) | 0 / 102 (0.00%) |
| occurrences (all) | 2 | 3 | 0 |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | |
|---|---|---|---|
| Cough | | | |
| subjects affected / exposed | 4 / 55 (7.27%) | 14 / 98 (14.29%) | 18 / 102 (17.65%) |
| occurrences (all) | 8 | 16 | 23 |
| Nasal congestion | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 3 / 98 (3.06%) | 6 / 102 (5.88%) |
| occurrences (all) | 2 | 3 | 8 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 2 / 55 (3.64%) | 3 / 98 (3.06%) | 3 / 102 (2.94%) |
| occurrences (all) | 3 | 4 | 3 |
| Asthma | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 1 / 102 (0.98%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis diaper | | | |
| subjects affected / exposed | 2 / 55 (3.64%) | 4 / 98 (4.08%) | 5 / 102 (4.90%) |
| occurrences (all) | 2 | 4 | 7 |
| Eczema | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 8 / 98 (8.16%) | 4 / 102 (3.92%) |
| occurrences (all) | 1 | 10 | 4 |
| Dermatitis atopic | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 2 / 98 (2.04%) | 1 / 102 (0.98%) |
| occurrences (all) | 1 | 3 | 1 |
| Psychiatric disorders | | | |
| Sleep disorder | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 12 / 98 (12.24%) | 6 / 102 (5.88%) |
| occurrences (all) | 1 | 16 | 11 |
| Middle insomnia | | | |
| subjects affected / exposed | 3 / 55 (5.45%) | 6 / 98 (6.12%) | 4 / 102 (3.92%) |
| occurrences (all) | 3 | 7 | 4 |
| Insomnia | | | |
| subjects affected / exposed | 3 / 55 (5.45%) | 3 / 98 (3.06%) | 1 / 102 (0.98%) |
| occurrences (all) | 3 | 3 | 1 |
| Agitation | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 1 / 98 (1.02%) | 6 / 102 (5.88%) |
| occurrences (all) | 0 | 1 | 6 |
| Infections and infestations | | | |

| | | | |
|---|---|---|---|
| Nasopharyngitis | | | |
| subjects affected / exposed | 10 / 55 (18.18%) | 29 / 98 (29.59%) | 21 / 102 (20.59%) |
| occurrences (all) | 13 | 51 | 31 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 4 / 55 (7.27%) | 6 / 98 (6.12%) | 13 / 102 (12.75%) |
| occurrences (all) | 5 | 7 | 16 |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 5 / 98 (5.10%) | 8 / 102 (7.84%) |
| occurrences (all) | 1 | 8 | 8 |
| Gastroenteritis | | | |
| subjects affected / exposed | 2 / 55 (3.64%) | 2 / 98 (2.04%) | 5 / 102 (4.90%) |
| occurrences (all) | 2 | 3 | 5 |
| Bronchiolitis | | | |
| subjects affected / exposed | 3 / 55 (5.45%) | 5 / 98 (5.10%) | 7 / 102 (6.86%) |
| occurrences (all) | 3 | 8 | 8 |
| Rhinitis | | | |
| subjects affected / exposed | 5 / 55 (9.09%) | 13 / 98 (13.27%) | 13 / 102 (12.75%) |
| occurrences (all) | 5 | 16 | 13 |
| Ear infection | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 7 / 98 (7.14%) | 6 / 102 (5.88%) |
| occurrences (all) | 0 | 9 | 6 |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 1 / 98 (1.02%) | 0 / 102 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Pharyngitis | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 4 / 98 (4.08%) | 3 / 102 (2.94%) |
| occurrences (all) | 0 | 5 | 3 |
| Otitis media | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 1 / 98 (1.02%) | 1 / 102 (0.98%) |
| occurrences (all) | 0 | 1 | 1 |
| Influenza | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 1 / 98 (1.02%) | 3 / 102 (2.94%) |
| occurrences (all) | 1 | 1 | 3 |
| Varicella | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |

| | | | |
|---|---|---|---|
| Roseola | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 1 / 98 (1.02%) | 0 / 102 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Hand-foot-and-mouth disease | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Acute tonsillitis | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Croup infectious | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 1 / 98 (1.02%) | 1 / 102 (0.98%) |
| occurrences (all) | 0 | 2 | 1 |
| Eye Infection | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 0 / 98 (0.00%) | 1 / 102 (0.98%) |
| occurrences (all) | 1 | 0 | 1 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 55 (0.00%) | 0 / 98 (0.00%) | 0 / 102 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 1 / 55 (1.82%) | 5 / 98 (5.10%) | 3 / 102 (2.94%) |
| occurrences (all) | 1 | 6 | 3 |

| **Non-serious adverse events** | W24-treatment period-safety set-3mg/kg/D,3months | W24-treatment period-safety set-3mg/kg/D,6months | W72-follow-up period of placebo group-safety set |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 92 / 100 (92.00%) | 96 / 101 (95.05%) | 27 / 33 (81.82%) |
| Injury, poisoning and procedural complications | | | |
| Vaccination complication | | | |
| subjects affected / exposed | 8 / 100 (8.00%) | 8 / 101 (7.92%) | 1 / 33 (3.03%) |
| occurrences (all) | 8 | 9 | 2 |
| Vascular disorders | | | |
| Peripheral coldness | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 10 / 101 (9.90%) | 0 / 33 (0.00%) |
| occurrences (all) | 1 | 10 | 0 |
| Nervous system disorders | | | |

| | | | |
|---|---|---|---|
| Somnolence | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 1 / 101 (0.99%) | 0 / 33 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Hypotonia | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 2 / 33 (6.06%) |
| occurrences (all) | 0 | 0 | 2 |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 22 / 100 (22.00%) | 28 / 101 (27.72%) | 6 / 33 (18.18%) |
| occurrences (all) | 34 | 36 | 16 |
| Irritability | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 2 / 101 (1.98%) | 0 / 33 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Condition aggravated | | | |
| subjects affected / exposed | 3 / 100 (3.00%) | 2 / 101 (1.98%) | 2 / 33 (6.06%) |
| occurrences (all) | 3 | 2 | 3 |
| Eye disorders | | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 2 / 100 (2.00%) | 8 / 101 (7.92%) | 1 / 33 (3.03%) |
| occurrences (all) | 2 | 10 | 1 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 17 / 100 (17.00%) | 28 / 101 (27.72%) | 1 / 33 (3.03%) |
| occurrences (all) | 20 | 51 | 1 |
| Teething | | | |
| subjects affected / exposed | 16 / 100 (16.00%) | 22 / 101 (21.78%) | 0 / 33 (0.00%) |
| occurrences (all) | 25 | 34 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 10 / 100 (10.00%) | 13 / 101 (12.87%) | 2 / 33 (6.06%) |
| occurrences (all) | 11 | 25 | 2 |
| Toothache | | | |
| subjects affected / exposed | 8 / 100 (8.00%) | 10 / 101 (9.90%) | 0 / 33 (0.00%) |
| occurrences (all) | 14 | 12 | 0 |
| Constipation | | | |
| subjects affected / exposed | 9 / 100 (9.00%) | 4 / 101 (3.96%) | 1 / 33 (3.03%) |
| occurrences (all) | 11 | 4 | 1 |

| | | | |
|---|---|---|---|
| Gingival pain | | | |
| subjects affected / exposed | 5 / 100 (5.00%) | 2 / 101 (1.98%) | 1 / 33 (3.03%) |
| occurrences (all) | 9 | 2 | 1 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 16 / 100 (16.00%) | 14 / 101 (13.86%) | 4 / 33 (12.12%) |
| occurrences (all) | 22 | 22 | 5 |
| Nasal congestion | | | |
| subjects affected / exposed | 4 / 100 (4.00%) | 4 / 101 (3.96%) | 0 / 33 (0.00%) |
| occurrences (all) | 6 | 8 | 0 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 8 / 100 (8.00%) | 3 / 101 (2.97%) | 0 / 33 (0.00%) |
| occurrences (all) | 13 | 3 | 0 |
| Asthma | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 2 / 101 (1.98%) | 0 / 33 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis diaper | | | |
| subjects affected / exposed | 4 / 100 (4.00%) | 9 / 101 (8.91%) | 1 / 33 (3.03%) |
| occurrences (all) | 5 | 13 | 1 |
| Eczema | | | |
| subjects affected / exposed | 2 / 100 (2.00%) | 2 / 101 (1.98%) | 2 / 33 (6.06%) |
| occurrences (all) | 2 | 2 | 2 |
| Dermatitis atopic | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 3 / 101 (2.97%) | 2 / 33 (6.06%) |
| occurrences (all) | 1 | 3 | 2 |
| Psychiatric disorders | | | |
| Sleep disorder | | | |
| subjects affected / exposed | 1 / 100 (1.00%) | 7 / 101 (6.93%) | 1 / 33 (3.03%) |
| occurrences (all) | 1 | 8 | 1 |
| Middle insomnia | | | |
| subjects affected / exposed | 7 / 100 (7.00%) | 6 / 101 (5.94%) | 0 / 33 (0.00%) |
| occurrences (all) | 7 | 10 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 3 / 100 (3.00%) | 3 / 101 (2.97%) | 1 / 33 (3.03%) |
| occurrences (all) | 3 | 3 | 1 |

| | | | |
|---|---|---|---|
| Agitation | | | |
| subjects affected / exposed | 3 / 100 (3.00%) | 0 / 101 (0.00%) | 0 / 33 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 32 / 100 (32.00%) | 34 / 101 (33.66%) | 8 / 33 (24.24%) |
| occurrences (all) | 51 | 47 | 13 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 20 / 100 (20.00%) | 16 / 101 (15.84%) | 5 / 33 (15.15%) |
| occurrences (all) | 28 | 19 | 8 |
| Bronchitis | | | |
| subjects affected / exposed | 10 / 100 (10.00%) | 16 / 101 (15.84%) | 3 / 33 (9.09%) |
| occurrences (all) | 15 | 22 | 5 |
| Gastroenteritis | | | |
| subjects affected / exposed | 4 / 100 (4.00%) | 11 / 101 (10.89%) | 4 / 33 (12.12%) |
| occurrences (all) | 4 | 11 | 4 |
| Bronchiolitis | | | |
| subjects affected / exposed | 5 / 100 (5.00%) | 9 / 101 (8.91%) | 2 / 33 (6.06%) |
| occurrences (all) | 6 | 12 | 3 |
| Rhinitis | | | |
| subjects affected / exposed | 5 / 100 (5.00%) | 5 / 101 (4.95%) | 3 / 33 (9.09%) |
| occurrences (all) | 5 | 6 | 4 |
| Ear infection | | | |
| subjects affected / exposed | 7 / 100 (7.00%) | 4 / 101 (3.96%) | 6 / 33 (18.18%) |
| occurrences (all) | 13 | 6 | 11 |
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 3 / 33 (9.09%) |
| occurrences (all) | 0 | 0 | 3 |
| Pharyngitis | | | |
| subjects affected / exposed | 2 / 100 (2.00%) | 3 / 101 (2.97%) | 0 / 33 (0.00%) |
| occurrences (all) | 2 | 3 | 0 |
| Otitis media | | | |
| subjects affected / exposed | 3 / 100 (3.00%) | 2 / 101 (1.98%) | 6 / 33 (18.18%) |
| occurrences (all) | 3 | 2 | 7 |
| Influenza | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 100 (3.00%) | 4 / 101 (3.96%) | 1 / 33 (3.03%) |
| occurrences (all) | 5 | 4 | 1 |
| Varicella | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 2 / 33 (6.06%) |
| occurrences (all) | 0 | 0 | 2 |
| Roseola | | | |
| subjects affected / exposed | 2 / 100 (2.00%) | 0 / 101 (0.00%) | 1 / 33 (3.03%) |
| occurrences (all) | 2 | 0 | 1 |
| Hand-foot-and-mouth disease | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 2 / 33 (6.06%) |
| occurrences (all) | 0 | 0 | 2 |
| Acute tonsillitis | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 2 / 101 (1.98%) | 2 / 33 (6.06%) |
| occurrences (all) | 0 | 2 | 3 |
| Croup infectious | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 1 / 101 (0.99%) | 2 / 33 (6.06%) |
| occurrences (all) | 0 | 1 | 2 |
| Eye Infection | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 0 / 101 (0.00%) | 3 / 33 (9.09%) |
| occurrences (all) | 0 | 0 | 3 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 100 (0.00%) | 1 / 101 (0.99%) | 2 / 33 (6.06%) |
| occurrences (all) | 0 | 1 | 2 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 5 / 100 (5.00%) | 1 / 101 (0.99%) | 0 / 33 (0.00%) |
| occurrences (all) | 5 | 1 | 0 |

| **Non-serious adverse events** | W72-follow-up period of 1mg/kg/D,3months group-safety set | W72-follow-up period of 1mg/kg/D,6months group-safety set | W72-follow-up period of 3mg/kg/D,3months group-safety set |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 66 / 85 (77.65%) | 70 / 91 (76.92%) | 65 / 87 (74.71%) |
| Injury, poisoning and procedural complications | | | |
| Vaccination complication | | | |
| subjects affected / exposed | 1 / 85 (1.18%) | 1 / 91 (1.10%) | 2 / 87 (2.30%) |
| occurrences (all) | 1 | 1 | 2 |

| | | | |
|---|---|---|---|
| Vascular disorders | | | |
| Peripheral coldness | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 0 / 87 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nervous system disorders | | | |
| Somnolence | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 0 / 87 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hypotonia | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 0 / 87 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 21 / 85 (24.71%) | 15 / 91 (16.48%) | 20 / 87 (22.99%) |
| occurrences (all) | 31 | 24 | 41 |
| Irritability | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 1 / 91 (1.10%) | 0 / 87 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Condition aggravated | | | |
| subjects affected / exposed | 1 / 85 (1.18%) | 1 / 91 (1.10%) | 1 / 87 (1.15%) |
| occurrences (all) | 1 | 1 | 1 |
| Eye disorders | | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 7 / 85 (8.24%) | 8 / 91 (8.79%) | 7 / 87 (8.05%) |
| occurrences (all) | 9 | 12 | 11 |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 4 / 85 (4.71%) | 4 / 91 (4.40%) | 10 / 87 (11.49%) |
| occurrences (all) | 4 | 4 | 13 |
| Teething | | | |
| subjects affected / exposed | 5 / 85 (5.88%) | 9 / 91 (9.89%) | 7 / 87 (8.05%) |
| occurrences (all) | 5 | 15 | 15 |
| Vomiting | | | |
| subjects affected / exposed | 3 / 85 (3.53%) | 3 / 91 (3.30%) | 4 / 87 (4.60%) |
| occurrences (all) | 3 | 3 | 5 |
| Toothache | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 85 (1.18%) | 0 / 91 (0.00%) | 0 / 87 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Constipation | | | |
| subjects affected / exposed | 1 / 85 (1.18%) | 4 / 91 (4.40%) | 0 / 87 (0.00%) |
| occurrences (all) | 1 | 4 | 0 |
| Gingival pain | | | |
| subjects affected / exposed | 1 / 85 (1.18%) | 0 / 91 (0.00%) | 1 / 87 (1.15%) |
| occurrences (all) | 1 | 0 | 1 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 8 / 85 (9.41%) | 5 / 91 (5.49%) | 7 / 87 (8.05%) |
| occurrences (all) | 14 | 6 | 9 |
| Nasal congestion | | | |
| subjects affected / exposed | 1 / 85 (1.18%) | 1 / 91 (1.10%) | 0 / 87 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 3 / 87 (3.45%) |
| occurrences (all) | 0 | 0 | 6 |
| Asthma | | | |
| subjects affected / exposed | 2 / 85 (2.35%) | 3 / 91 (3.30%) | 5 / 87 (5.75%) |
| occurrences (all) | 4 | 3 | 12 |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis diaper | | | |
| subjects affected / exposed | 4 / 85 (4.71%) | 2 / 91 (2.20%) | 3 / 87 (3.45%) |
| occurrences (all) | 4 | 2 | 3 |
| Eczema | | | |
| subjects affected / exposed | 4 / 85 (4.71%) | 2 / 91 (2.20%) | 4 / 87 (4.60%) |
| occurrences (all) | 4 | 3 | 4 |
| Dermatitis atopic | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 2 / 87 (2.30%) |
| occurrences (all) | 0 | 0 | 2 |
| Psychiatric disorders | | | |
| Sleep disorder | | | |
| subjects affected / exposed | 1 / 85 (1.18%) | 0 / 91 (0.00%) | 1 / 87 (1.15%) |
| occurrences (all) | 1 | 0 | 1 |
| Middle insomnia | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 0 / 87 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Insomnia | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 0 / 87 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Agitation | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 0 / 87 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 26 / 85 (30.59%) | 20 / 91 (21.98%) | 24 / 87 (27.59%) |
| occurrences (all) | 45 | 27 | 39 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 7 / 85 (8.24%) | 15 / 91 (16.48%) | 13 / 87 (14.94%) |
| occurrences (all) | 12 | 27 | 21 |
| Bronchitis | | | |
| subjects affected / exposed | 12 / 85 (14.12%) | 14 / 91 (15.38%) | 18 / 87 (20.69%) |
| occurrences (all) | 24 | 18 | 28 |
| Gastroenteritis | | | |
| subjects affected / exposed | 7 / 85 (8.24%) | 9 / 91 (9.89%) | 14 / 87 (16.09%) |
| occurrences (all) | 8 | 9 | 15 |
| Bronchiolitis | | | |
| subjects affected / exposed | 6 / 85 (7.06%) | 4 / 91 (4.40%) | 9 / 87 (10.34%) |
| occurrences (all) | 6 | 4 | 14 |
| Rhinitis | | | |
| subjects affected / exposed | 9 / 85 (10.59%) | 7 / 91 (7.69%) | 1 / 87 (1.15%) |
| occurrences (all) | 14 | 13 | 1 |
| Ear infection | | | |
| subjects affected / exposed | 13 / 85 (15.29%) | 13 / 91 (14.29%) | 14 / 87 (16.09%) |
| occurrences (all) | 30 | 23 | 28 |
| Tonsillitis | | | |
| subjects affected / exposed | 7 / 85 (8.24%) | 6 / 91 (6.59%) | 7 / 87 (8.05%) |
| occurrences (all) | 12 | 8 | 10 |
| Pharyngitis | | | |
| subjects affected / exposed | 5 / 85 (5.88%) | 4 / 91 (4.40%) | 6 / 87 (6.90%) |
| occurrences (all) | 8 | 4 | 7 |

| | | | |
|---|---|---|---|
| Otitis media | | | |
| subjects affected / exposed | 5 / 85 (5.88%) | 4 / 91 (4.40%) | 4 / 87 (4.60%) |
| occurrences (all) | 6 | 6 | 8 |
| Influenza | | | |
| subjects affected / exposed | 2 / 85 (2.35%) | 0 / 91 (0.00%) | 2 / 87 (2.30%) |
| occurrences (all) | 2 | 0 | 2 |
| Varicella | | | |
| subjects affected / exposed | 5 / 85 (5.88%) | 4 / 91 (4.40%) | 6 / 87 (6.90%) |
| occurrences (all) | 5 | 5 | 6 |
| Roseola | | | |
| subjects affected / exposed | 3 / 85 (3.53%) | 5 / 91 (5.49%) | 1 / 87 (1.15%) |
| occurrences (all) | 3 | 5 | 1 |
| Hand-foot-and-mouth disease | | | |
| subjects affected / exposed | 1 / 85 (1.18%) | 2 / 91 (2.20%) | 3 / 87 (3.45%) |
| occurrences (all) | 1 | 2 | 3 |
| Acute tonsillitis | | | |
| subjects affected / exposed | 1 / 85 (1.18%) | 0 / 91 (0.00%) | 1 / 87 (1.15%) |
| occurrences (all) | 1 | 0 | 1 |
| Croup infectious | | | |
| subjects affected / exposed | 1 / 85 (1.18%) | 1 / 91 (1.10%) | 1 / 87 (1.15%) |
| occurrences (all) | 1 | 1 | 1 |
| Eye Infection | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 0 / 91 (0.00%) | 1 / 87 (1.15%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 1 / 85 (1.18%) | 0 / 91 (0.00%) | 0 / 87 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 0 / 85 (0.00%) | 1 / 91 (1.10%) | 0 / 87 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |

| **Non-serious adverse events** | W72-follow-up period of 3mg/kg/D,6months group-safety set | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 75 / 95 (78.95%) | | |

| | | | |
|---|---|---|---|
| Injury, poisoning and procedural complications | | | |
| Vaccination complication | | | |
| subjects affected / exposed | 2 / 95 (2.11%) | | |
| occurrences (all) | 2 | | |
| Vascular disorders | | | |
| Peripheral coldness | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | |
| occurrences (all) | 0 | | |
| Nervous system disorders | | | |
| Somnolence | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hypotonia | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | |
| occurrences (all) | 0 | | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 24 / 95 (25.26%) | | |
| occurrences (all) | 36 | | |
| Irritability | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | |
| occurrences (all) | 0 | | |
| Condition aggravated | | | |
| subjects affected / exposed | 3 / 95 (3.16%) | | |
| occurrences (all) | 3 | | |
| Eye disorders | | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 9 / 95 (9.47%) | | |
| occurrences (all) | 10 | | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 9 / 95 (9.47%) | | |
| occurrences (all) | 9 | | |
| Teething | | | |
| subjects affected / exposed | 8 / 95 (8.42%) | | |
| occurrences (all) | 13 | | |
| Vomiting | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 95 (2.11%) | | |
| occurrences (all) | 3 | | |
| Toothache | | | |
| subjects affected / exposed | 4 / 95 (4.21%) | | |
| occurrences (all) | 6 | | |
| Constipation | | | |
| subjects affected / exposed | 1 / 95 (1.05%) | | |
| occurrences (all) | 1 | | |
| Gingival pain | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | |
| occurrences (all) | 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Cough | | | |
| subjects affected / exposed | 7 / 95 (7.37%) | | |
| occurrences (all) | 8 | | |
| Nasal congestion | | | |
| subjects affected / exposed | 1 / 95 (1.05%) | | |
| occurrences (all) | 2 | | |
| Rhinorrhoea | | | |
| subjects affected / exposed | 5 / 95 (5.26%) | | |
| occurrences (all) | 6 | | |
| Asthma | | | |
| subjects affected / exposed | 5 / 95 (5.26%) | | |
| occurrences (all) | 7 | | |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis diaper | | | |
| subjects affected / exposed | 3 / 95 (3.16%) | | |
| occurrences (all) | 3 | | |
| Eczema | | | |
| subjects affected / exposed | 4 / 95 (4.21%) | | |
| occurrences (all) | 4 | | |
| Dermatitis atopic | | | |
| subjects affected / exposed | 2 / 95 (2.11%) | | |
| occurrences (all) | 3 | | |
| Psychiatric disorders | | | |

| | | | |
|---|---|---|---|
| Sleep disorder | | | |
| subjects affected / exposed | 1 / 95 (1.05%) | | |
| occurrences (all) | 1 | | |
| Middle insomnia | | | |
| subjects affected / exposed | 1 / 95 (1.05%) | | |
| occurrences (all) | 1 | | |
| Insomnia | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | |
| occurrences (all) | 0 | | |
| Agitation | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | |
| occurrences (all) | 0 | | |
| Infections and infestations | | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 30 / 95 (31.58%) | | |
| occurrences (all) | 50 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 11 / 95 (11.58%) | | |
| occurrences (all) | 16 | | |
| Bronchitis | | | |
| subjects affected / exposed | 20 / 95 (21.05%) | | |
| occurrences (all) | 34 | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 14 / 95 (14.74%) | | |
| occurrences (all) | 16 | | |
| Bronchiolitis | | | |
| subjects affected / exposed | 11 / 95 (11.58%) | | |
| occurrences (all) | 14 | | |
| Rhinitis | | | |
| subjects affected / exposed | 6 / 95 (6.32%) | | |
| occurrences (all) | 10 | | |
| Ear infection | | | |
| subjects affected / exposed | 17 / 95 (17.89%) | | |
| occurrences (all) | 37 | | |
| Tonsillitis | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 10 / 95 (10.53%) | | |
| occurrences (all) | 13 | | |
| Pharyngitis | | | |
| subjects affected / exposed | 8 / 95 (8.42%) | | |
| occurrences (all) | 13 | | |
| Otitis media | | | |
| subjects affected / exposed | 5 / 95 (5.26%) | | |
| occurrences (all) | 6 | | |
| Influenza | | | |
| subjects affected / exposed | 5 / 95 (5.26%) | | |
| occurrences (all) | 6 | | |
| Varicella | | | |
| subjects affected / exposed | 4 / 95 (4.21%) | | |
| occurrences (all) | 4 | | |
| Roseola | | | |
| subjects affected / exposed | 4 / 95 (4.21%) | | |
| occurrences (all) | 4 | | |
| Hand-foot-and-mouth disease | | | |
| subjects affected / exposed | 3 / 95 (3.16%) | | |
| occurrences (all) | 5 | | |
| Acute tonsillitis | | | |
| subjects affected / exposed | 2 / 95 (2.11%) | | |
| occurrences (all) | 2 | | |
| Croup infectious | | | |
| subjects affected / exposed | 1 / 95 (1.05%) | | |
| occurrences (all) | 1 | | |
| Eye Infection | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 95 (0.00%) | | |
| occurrences (all) | 0 | | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 1 / 95 (1.05%) | | |
| occurrences (all) | 1 | | |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 31 August 2010 | Changes discussed with and agreed by the FDA and the EMEA:<br>- Reduction of the number of patients/placebo arm<br>- Extension from facial to non-facial IH<br>- Suppression of the 50:50 balance USA/EU<br>- Clarifications concerning monitoring process and statistical analysis. |
| 21 September 2010 | Local to Czech Repulic to comply with the Czech rules :<br>Addition of an exclusion criteria - Exclusion of patients in whom a systemic corticosteroid treatment was the most advisable therapy in the opinion of the Investigator. |
| 29 November 2010 | - Clarification of the list of treatment (authorized and not authorized)<br>- Clarification of monitoring process linked to patient safety<br>- Modification according some national regulations. |
| 19 March 2012 | Clarification of pharmaceutical, monitoring, statistical process/analysis. |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported

### Online references

http://www.ncbi.nlm.nih.gov/pubmed/25693013