



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
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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)	EMA-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
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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
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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 Units: Subjects			

Age continuous Units: days arithmetic mean standard deviation	103.91 ± 31.06	103.58 ± 33.07	102.65 ± 30.12
Gender categorical 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 Units: Subjects			

Age continuous Units: days arithmetic mean standard deviation	107.53 ± 30.14	101.63 ± 31	-
Gender categorical 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 Units: Subjects			

Age continuous Units: days arithmetic mean standard deviation	103.85 ± 31.02	±	
Gender categorical 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 comparison 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
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	13.1
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Reporting groups

Reporting group title	W24-treatment period-safety set- Placebo
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Reporting group description: -

Reporting group title	W24-treatment period-safety set-1mg/kg/D,3months
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Reporting group description: -

Reporting group title	W24-treatment period-safety set-1mg/kg/D,6months
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Reporting group description: -

Reporting group title	W24-treatment period-safety set-3mg/kg/D,3months
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Reporting group description: -

Reporting group title	W24-treatment period-safety set-3mg/kg/D,6months
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Reporting group description: -

Reporting group title	W72-follow-up period of placebo group-safety set
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Reporting group description: -

Reporting group title	W72-follow-up period of 1mg/kg/D,3months group-safety set
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Reporting group description: -

Reporting group title	W72-follow-up period of 1mg/kg/D,6months group-safety set
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Reporting group description: -

Reporting group title	W72-follow-up period of 3mg/kg/D,3months group-safety set
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Reporting group description: -

Reporting group title	W72-follow-up period of 3mg/kg/D,6months group-safety set
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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			
Gastroesophageal 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 occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 85 (0.00%) 0 / 0 0 / 0	 0 / 91 (0.00%) 0 / 0 0 / 0	 1 / 87 (1.15%) 0 / 1 0 / 0
Bronchitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 85 (1.18%) 0 / 1 0 / 0	 0 / 91 (0.00%) 0 / 0 0 / 0	 0 / 87 (0.00%) 0 / 0 0 / 0
Bronchopneumonia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 85 (0.00%) 0 / 0 0 / 0	 0 / 91 (0.00%) 0 / 0 0 / 0	 0 / 87 (0.00%) 0 / 0 0 / 0
Cystitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 85 (0.00%) 0 / 0 0 / 0	 0 / 91 (0.00%) 0 / 0 0 / 0	 0 / 87 (0.00%) 0 / 0 0 / 0
Gastroenteritis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 85 (0.00%) 0 / 0 0 / 0	 0 / 91 (0.00%) 0 / 0 0 / 0	 0 / 87 (0.00%) 0 / 0 0 / 0
Pyelonephritis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 85 (0.00%) 0 / 0 0 / 0	 0 / 91 (0.00%) 0 / 0 0 / 0	 0 / 87 (0.00%) 0 / 0 0 / 0
Rotavirus infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 1 / 85 (1.18%) 0 / 1 0 / 0	 0 / 91 (0.00%) 0 / 0 0 / 0	 2 / 87 (2.30%) 0 / 2 0 / 0
Viraemia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	 0 / 85 (0.00%) 0 / 0 0 / 0	 0 / 91 (0.00%) 0 / 0 0 / 0	 0 / 87 (0.00%) 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			
Gastroesophageal 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 occurrences (all)	0 / 55 (0.00%) 0	1 / 98 (1.02%) 1	1 / 102 (0.98%) 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 occurrences (all)	4 / 55 (7.27%) 8	14 / 98 (14.29%) 16	18 / 102 (17.65%) 23
Nasal congestion subjects affected / exposed occurrences (all)	1 / 55 (1.82%) 2	3 / 98 (3.06%) 3	6 / 102 (5.88%) 8
Rhinorrhoea subjects affected / exposed occurrences (all)	2 / 55 (3.64%) 3	3 / 98 (3.06%) 4	3 / 102 (2.94%) 3
Asthma subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	0 / 98 (0.00%) 0	1 / 102 (0.98%) 1
Skin and subcutaneous tissue disorders			
Dermatitis diaper subjects affected / exposed occurrences (all)	2 / 55 (3.64%) 2	4 / 98 (4.08%) 4	5 / 102 (4.90%) 7
Eczema subjects affected / exposed occurrences (all)	1 / 55 (1.82%) 1	8 / 98 (8.16%) 10	4 / 102 (3.92%) 4
Dermatitis atopic subjects affected / exposed occurrences (all)	1 / 55 (1.82%) 1	2 / 98 (2.04%) 3	1 / 102 (0.98%) 1
Psychiatric disorders			
Sleep disorder subjects affected / exposed occurrences (all)	1 / 55 (1.82%) 1	12 / 98 (12.24%) 16	6 / 102 (5.88%) 11
Middle insomnia subjects affected / exposed occurrences (all)	3 / 55 (5.45%) 3	6 / 98 (6.12%) 7	4 / 102 (3.92%) 4
Insomnia subjects affected / exposed occurrences (all)	3 / 55 (5.45%) 3	3 / 98 (3.06%) 3	1 / 102 (0.98%) 1
Agitation subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0	1 / 98 (1.02%) 1	6 / 102 (5.88%) 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 occurrences (all)	1 / 100 (1.00%) 1	1 / 101 (0.99%) 1	0 / 33 (0.00%) 0
Hypotonia subjects affected / exposed occurrences (all)	0 / 100 (0.00%) 0	0 / 101 (0.00%) 0	2 / 33 (6.06%) 2
General disorders and administration site conditions			
Pyrexia subjects affected / exposed occurrences (all)	22 / 100 (22.00%) 34	28 / 101 (27.72%) 36	6 / 33 (18.18%) 16
Irritability subjects affected / exposed occurrences (all)	1 / 100 (1.00%) 1	2 / 101 (1.98%) 2	0 / 33 (0.00%) 0
Condition aggravated subjects affected / exposed occurrences (all)	3 / 100 (3.00%) 3	2 / 101 (1.98%) 2	2 / 33 (6.06%) 3
Eye disorders			
Conjunctivitis subjects affected / exposed occurrences (all)	2 / 100 (2.00%) 2	8 / 101 (7.92%) 10	1 / 33 (3.03%) 1
Gastrointestinal disorders			
Diarrhoea subjects affected / exposed occurrences (all)	17 / 100 (17.00%) 20	28 / 101 (27.72%) 51	1 / 33 (3.03%) 1
Teething subjects affected / exposed occurrences (all)	16 / 100 (16.00%) 25	22 / 101 (21.78%) 34	0 / 33 (0.00%) 0
Vomiting subjects affected / exposed occurrences (all)	10 / 100 (10.00%) 11	13 / 101 (12.87%) 25	2 / 33 (6.06%) 2
Toothache subjects affected / exposed occurrences (all)	8 / 100 (8.00%) 14	10 / 101 (9.90%) 12	0 / 33 (0.00%) 0
Constipation subjects affected / exposed occurrences (all)	9 / 100 (9.00%) 11	4 / 101 (3.96%) 4	1 / 33 (3.03%) 1

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

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

subjects affected / exposed occurrences (all)	3 / 100 (3.00%) 5	4 / 101 (3.96%) 4	1 / 33 (3.03%) 1
Varicella subjects affected / exposed occurrences (all)	0 / 100 (0.00%) 0	0 / 101 (0.00%) 0	2 / 33 (6.06%) 2
Roseola subjects affected / exposed occurrences (all)	2 / 100 (2.00%) 2	0 / 101 (0.00%) 0	1 / 33 (3.03%) 1
Hand-foot-and-mouth disease subjects affected / exposed occurrences (all)	0 / 100 (0.00%) 0	0 / 101 (0.00%) 0	2 / 33 (6.06%) 2
Acute tonsillitis subjects affected / exposed occurrences (all)	0 / 100 (0.00%) 0	2 / 101 (1.98%) 2	2 / 33 (6.06%) 3
Croup infectious subjects affected / exposed occurrences (all)	0 / 100 (0.00%) 0	1 / 101 (0.99%) 1	2 / 33 (6.06%) 2
Eye Infection subjects affected / exposed occurrences (all)	0 / 100 (0.00%) 0	0 / 101 (0.00%) 0	3 / 33 (9.09%) 3
Gastroenteritis viral subjects affected / exposed occurrences (all)	0 / 100 (0.00%) 0	1 / 101 (0.99%) 1	2 / 33 (6.06%) 2
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	5 / 100 (5.00%) 5	1 / 101 (0.99%) 1	0 / 33 (0.00%) 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 occurrences (all)	1 / 85 (1.18%) 1	1 / 91 (1.10%) 1	2 / 87 (2.30%) 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 occurrences (all)	2 / 95 (2.11%) 2		
Vascular disorders Peripheral coldness subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0		
Nervous system disorders Somnolence subjects affected / exposed occurrences (all) Hypotonia subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0 0 / 95 (0.00%) 0		
General disorders and administration site conditions Pyrexia subjects affected / exposed occurrences (all) Irritability subjects affected / exposed occurrences (all) Condition aggravated subjects affected / exposed occurrences (all)	24 / 95 (25.26%) 36 0 / 95 (0.00%) 0 3 / 95 (3.16%) 3		
Eye disorders Conjunctivitis subjects affected / exposed occurrences (all)	9 / 95 (9.47%) 10		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Teething subjects affected / exposed occurrences (all) Vomiting	9 / 95 (9.47%) 9 8 / 95 (8.42%) 13		

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

Sleep disorder subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1		
Middle insomnia subjects affected / exposed occurrences (all)	1 / 95 (1.05%) 1		
Insomnia subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0		
Agitation subjects affected / exposed occurrences (all)	0 / 95 (0.00%) 0		
Infections and infestations			
Nasopharyngitis subjects affected / exposed occurrences (all)	30 / 95 (31.58%) 50		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	11 / 95 (11.58%) 16		
Bronchitis subjects affected / exposed occurrences (all)	20 / 95 (21.05%) 34		
Gastroenteritis subjects affected / exposed occurrences (all)	14 / 95 (14.74%) 16		
Bronchiolitis subjects affected / exposed occurrences (all)	11 / 95 (11.58%) 14		
Rhinitis subjects affected / exposed occurrences (all)	6 / 95 (6.32%) 10		
Ear infection subjects affected / exposed occurrences (all)	17 / 95 (17.89%) 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: <ul style="list-style-type: none">- Reduction of the number of patients/placebo arm- Extension from facial to non-facial IH- Suppression of the 50:50 balance USA/EU- Clarifications concerning monitoring process and statistical analysis.
21 September 2010	Local to Czech Republic to comply with the Czech rules : 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	<ul style="list-style-type: none">- Clarification of the list of treatment (authorized and not authorized)- Clarification of monitoring process linked to patient safety- 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>