Clinical trial results:
A Long Term Study of M071754 - An Open-Label Study in Patients With Infantile Spasms

Summary

EudraCT number	2017-000611-17
Trial protocol	Outside EU/EEA
Global end of trial date	30 November 2016

Results information

Result version number	v1 (current)
This version publication date	10 November 2017
First version publication date	10 November 2017

Trial information

Trial identification

Sponsor protocol code	LTS12745

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	Japan Pharmaceutical Information Center: JapicCTI-142559

Notes:

Sponsors

Sponsor organisation name	Alfresa Pharma Corporation
Sponsor organisation address	2-2-9 Kokumachi, Chuo-ku, Osaka , Japan, 540-8575
Public contact	Executive Officer, Alfresa Pharma Corporation, contact-suishin-1@kaihatsu-alfresa-pharma.com
Scientific contact	Executive Officer, Alfresa Pharma Corporation, contact-suishin-1@kaihatsu-alfresa-pharma.com
Sponsor organisation name	Sanofi K.K.
Sponsor organisation address	3-20-2 Nishi-Shinjuku, Shinjuku-ku, Tokyo , Japan, 163-1488
Public contact	Trial Transparency Team, Sanofi aventis recherche & développement, contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi aventis recherche & développement, contact-US@sanofi.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	01 March 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	30 November 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety of long-term administration of vigabatrin in subjects with infantile spasms and also to evaluate treatment efficacy.

Protection of trial subjects:

The study was conducted by investigators experienced in the treatment of pediatric patients. The parent(s) or guardian(s) as well as the children were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time. In addition to the consent form for the parent(s)/guardian(s), an assent form in child-appropriate language was provided and explained to the child. Repeated invasive procedures were minimized. The number of blood samples as well as the amount of blood drawn were adjusted according to age and weight. A topical anesthesia may have been used to minimize distress and discomfort.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	31 January 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Japan: 17
Worldwide total number of subjects	17
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	6
Children (2-11 years)	11

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:

The study was conducted at 6 centers in Japan from 31 January 2013 to 30 November 2016. A total of 17 subjects were enrolled and treated in the study.

Pre-assignment

Screening details:

The study consisted of 5 phases: a screening phase, a dose adjustment phase, a maintenance administration phase, a dose tapering phase, and a follow-up phase.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Vigabatrin

Arm description:

Vigabatrin 50 mg/kg/day to 150 mg/kg/day up to a maximum of 3 g/day, administered during dose adjustment phase (3 days - 8 weeks), followed by maintenance administration phase until switched to commercial formulation. In the event of no improvement in seizures or deterioration in seizure symptoms despite dose of 150 mg/kg/day up to a maximum of 3 g/day, subjects were moved to dose tapering phase (3 weeks).

Arm type	Experimental
Investigational medicinal product name	Vigabatrin
Investigational medicinal product code	M071754
Other name	
Pharmaceutical forms	Granules for oral solution in sachet
Routes of administration	Oral use

Dosage and administration details:

Dose adjustment phase: Vigabatrin 50 mg/kg/day (25 mg/kg/day twice a day) as initial dose; dose increased on Day 4 to 6 by 25-50 mg/kg/day, if seizures had not resolved and there was no safety concern. Thereafter, similar dose increments until seizures resolved or until a maximum dose of 150 mg/kg/day (75 mg/kg twice a day; up to a maximum of 3 g/day). Maintenance administration phase: subjects receiving appropriate dose in dose adjustment period or who reached a dose of 150 mg/kg/day (75 mg/kg/day twice a day; up to a maximum of 3 g/day) continued in maintenance administration phase at the same dose until switched to commercial formulation. Dose tapering phase: unless immediate discontinuation of vigabatrin or switched to commercial formulation, the dose was tapered by 25-50 mg/kg/day every 3-4 days over a 3 week period.

Number of subjects in period 1	Vigabatrin
Started	17
Entered Maintenance Phase	15
Completed 32 weeks	12
Completed 56 weeks	9
Completed	8
Not completed	9

Adverse event	2
Changed to other medication	7

Baseline characteristics

Reporting groups	
Reporting group title	Vigabatrin

Reporting group description:

Vigabatrin 50 mg/kg/day to 150 mg/kg/day up to a maximum of 3 g/day, administered during dose adjustment phase (3 days - 8 weeks), followed by maintenance administration phase until switched to commercial formulation. In the event of no improvement in seizures or deterioration in seizure symptoms despite dose of 150 mg/kg/day up to a maximum of 3 g/day, subjects were moved to dose tapering phase (3 weeks).

Reporting group values	Vigabatrin	Total	
Number of subjects	17	17	
Age categorical Units: Subjects			
Age continuous Units: months			
arithmetic mean	31.1		
standard deviation	± 18.4	-	
Gender categorical Units: Subjects			
Female	9	9	
Male	8	8	
Aetiology of infantile spasms Units: Subjects			
Brain malformation	1	1	
Neurocutaneous syndrome	8	8	
Metabolic abnormality	0	0	
Chromosomal/genetic abnormality	1	1	
Perinatal disorder	1	1	
Sequela to encephalitis/meningitis	0	0	
Sequela to encephalopathy	0	0	
Unknown	6	6	
Basis for diagnosis of infantile spasms: Series formation Units: Subjects			
Spasms - Series formation: Yes	17	17	
Spasms - Series formation: No	0	0	
Basis for diagnosis of infantile spasms: Hypsarrhythmia Units: Subjects			
Hypsarrhythmia: Yes	14	14	
Hypsarrhythmia: No	3	3	
Basis for diagnosis of infantile spasms: Developmental regression Units: Subjects			
Developmental regression: Yes	17	17	
Developmental regression: No	0	0	

End points

End points reporting groups

Reporting group title	Vigabatrin

Reporting group description:

Vigabatrin 50 mg/kg/day to 150 mg/kg/day up to a maximum of 3 g/day, administered during dose adjustment phase (3 days - 8 weeks), followed by maintenance administration phase until switched to commercial formulation. In the event of no improvement in seizures or deterioration in seizure symptoms despite dose of 150 mg/kg/day up to a maximum of 3 g/day, subjects were moved to dose tapering phase (3 weeks).

Primary: Number of Subjects With Abnormalities Finding

End point title	Number of Subjects With Abnormalities Finding[1]

End point description:

Number of subjects with abnormalities in laboratory tests (hematological tests, blood biochemical tests, urinalysis), ophthalmologic examinations, vital signs, 12-lead electrocardiography (ECG) and magnetic resonance imaging (MRI) examinations were reported. Analysis was performed on safety analysis set that included all subjects who were treated with investigational drug.

End point type	Primary

End point timeframe:

Baseline up to maximum of 184 weeks

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	Vigabatrin			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: subjects				
Laboratory Test abnormalities	9			
Ophthalmologic Examinations abnormalities	6			
Vital Signs abnormalities	1			
ECG abnormalities	3			
MRI Examinations abnormalities	2			

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Adverse Events (AEs) And Serious Adverse Events (SAEs)

End point title	Number of Subjects With Adverse Events (AEs) And Serious Adverse Events (SAEs)[2]

End point description:

AE: any untoward medical occurrence in a subject during the study; the event does not necessarily have a causal relationship with the treatment. This includes any newly occurring event or previous condition that has increased in severity or frequency after the informed consent form is signed. AE includes

serious as well as non-serious AEs. SAE (subset of AE): medical event or condition, which falls into any of the following categories, regardless of its relationship to the study drug: death, life threatening adverse experience, inpatient hospitalization/prolongation of hospitalization, persistent/significant disability or incapacity, congenital anomaly/birth defect, important medical event. Analysis was performed on safety analysis set.

End point type	Primary

End point timeframe:

Baseline up to maximum of 184 weeks

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	Vigabatrin			
Subject group type	Reporting group			
Number of subjects analysed	17			
Units: subjects				
AEs	17			
SAEs	6			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Reduction of At Least 50% From Baseline in Frequency of Spasms on Date of Assessment of Spasms

End point title	Percentage of Subjects With Reduction of At Least 50% From Baseline in Frequency of Spasms on Date of Assessment of Spasms

End point description:

Subjects who achieved at least 50% reduction from baseline in frequency of infantile spasms were reported in this endpoint. Analysis was performed on efficacy analysis set that included all subjects who were treated with the investigational drug. Here 'n' signifies number of subjects with available data for specified categories.

End point type	Secondary

End point timeframe:

Week 32 and Week 56 from start of maintenance administration phase

End point values	Vigabatrin			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: percentage of subjects				
number (confidence interval 95%)				
Week 32 (n=10)	90 (55.5 to 99.7)			
Week 56 (n=8)	100 (63.1 to 100)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Disappearance of Spasms on Date of Assessment of Frequency of Spasms

End point title	Percentage of Subjects with Disappearance of Spasms on Date of Assessment of Frequency of Spasms

End point description:

Subjects whose spasms were disappeared were reported in this endpoint. Analysis was performed on efficacy analysis set. Here 'n' signifies number of subjects with available data for specified categories.

End point type	Secondary

End point timeframe:

Week 32 and Week 56 from start of maintenance administration phase

End point values	Vigabatrin			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: percentage of subjects				
number (confidence interval 95%)				
Week 32 (n=10) Week 56 (n=8)	60 (26.2 to 87.8) 37.5 (8.5 to 75.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Complete Disappearance of Infantile Spasms

End point title	Percentage of Subjects with Complete Disappearance of Infantile Spasms

End point description:

Subjects whose spasms had disappeared and whose brainwaves showed no signs of hypsarrhythmia, were reported as having complete disappearance of spasms. Analysis was performed on efficacy analysis set. Here 'n' signifies number of subjects with available data for specified categories.

End point type	Secondary

End point timeframe:

Week 32 and Week 56 from start of maintenance administration phase

End point values	Vigabatrin			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: percentage of subjects				
number (not applicable)				
Week 32 (n=10) Week 56 (n=8)	40 37.5			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Normal Central Brain wave Assessment

End point title	Percentage of Subjects with Normal Central Brain wave Assessment

End point description:

A contingency table was prepared for evaluations of brainwave findings (normal, abnormal) by examination period. Percentage of subjects with abnormal brainwave findings were not reported. Analysis was performed on efficacy analysis set. Here 'n' signifies number of subjects with available data for specified categories.

End point type	Secondary

End point timeframe:

Week 32 and Week 56 from start of maintenance administration phase

End point values	Vigabatrin			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: percentage of subjects				
number (not applicable)				
Week 32 (n=10) Week 56 (n=8)	20 0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Comprehensive Evaluation of Efficacy by Principal Investigator or Sub-Investigator Including Impression of Guardians

End point title	Percentage of Subjects With Comprehensive Evaluation of Efficacy by Principal Investigator or Sub-Investigator Including Impression of Guardians

End point description:

The comprehensive evaluation of efficacy of Vigabatrin as "effective or ineffective" by the Principal investigator or sub-investigators including the guardians' opinion for the subjects was evaluated. Analysis was performed on efficacy analysis set. Here 'n' signifies number of subjects with available data for specified categories.

End point type	Secondary

End point timeframe:

Week 32 and Week 56 from start of maintenance administration phase

End point values	Vigabatrin			
Subject group type	Reporting group			
Number of subjects analysed	14			
Units: percentage of subjects				
number (not applicable)				
Week 32: Effective (n=10)	90			
Week 32: Ineffective (n=10)	10			
Week 56: Effective (n=8)	100			
Week 56: Ineffective (n=8)	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs were collected from signature of the informed consent form up to the final visit (up to 184 weeks) regardless of seriousness or relationship to investigational product.

Adverse event reporting additional description:

Reported AEs are treatment-emergent adverse events that is AEs that developed/worsened during the 'on treatment period' (time from dose adjustment phase until follow up phase). Analysis was performed on safety analysis set.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	Vigabatrin

Reporting group description:

Vigabatrin 50 mg/kg/day to 150 mg/kg/day up to a maximum of 3 g/day, administered during dose adjustment phase (3 days - 8 weeks), followed by maintenance administration phase until switched to commercial formulation. In the event of no improvement in seizures or deterioration in seizure symptoms despite dose of 150 mg/kg/day up to a maximum of 3 g/day, subjects were moved to dose tapering phase (3 weeks).

Serious adverse events	Vigabatrin		
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 17 (35.29%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Investigations			
Nuclear Magnetic Resonance Imaging Abnormal			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Status Epilepticus			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Encephalopathy			

subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Varicocele			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Bronchiolitis			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	1 / 17 (5.88%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Vigabatrin		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 17 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Kidney Angiomyolipoma			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Vascular disorders			
Haemorrhage			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	7 / 17 (41.18%)		
occurrences (all)	19		
Crying			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Immune system disorders			
Seasonal Allergy			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	3		
Reproductive system and breast disorders			
Balanoposthitis			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Upper Respiratory Tract Inflammation			

subjects affected / exposed occurrences (all)	5 / 17 (29.41%) 6		
Cough subjects affected / exposed occurrences (all)	2 / 17 (11.76%) 2		
Epistaxis subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Pneumonia Aspiration subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Rhinitis Allergic subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Rhinorrhoea subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 3		
Psychiatric disorders Agitation subjects affected / exposed occurrences (all)	5 / 17 (29.41%) 7		
Insomnia subjects affected / exposed occurrences (all)	2 / 17 (11.76%) 2		
Autism Spectrum Disorder subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Mood Altered subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Investigations C-Reactive Protein Increased subjects affected / exposed occurrences (all)	2 / 17 (11.76%) 2		
Laboratory Test Abnormal			

subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Retinogram Abnormal			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Alanine Aminotransferase Decreased			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Blood Alkaline Phosphatase Increased			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Blood Glucose Decreased			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Electroencephalogram Abnormal			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Glucose Urine Present			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Hepatic Enzyme Increased			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Arthropod Sting			
subjects affected / exposed	4 / 17 (23.53%)		
occurrences (all)	5		
Conjunctival Laceration			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Contusion			

subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Excoriation			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Lip Injury			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Nail Injury			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Thermal Burn			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Congenital, familial and genetic disorders			
Laryngomalacia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Cardiac disorders			
Bundle Branch Block Right			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Supraventricular Extrasystoles			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Nervous system disorders			
Somnolence			
subjects affected / exposed	3 / 17 (17.65%)		
occurrences (all)	3		
Cerebral Atrophy			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Dizziness			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	2		
Febrile Convulsion			

subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Hyperkinesia			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Eye disorders			
Chalazion			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Diarrhoea			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Stomatitis			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Vomiting			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Anal Fissure			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Enterocolitis			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Gastrooesophageal Reflux Disease			
subjects affected / exposed	1 / 17 (5.88%)		
occurrences (all)	1		
Hepatobiliary disorders			
Hepatic Function Abnormal			
subjects affected / exposed	2 / 17 (11.76%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			

Erythema				
subjects affected / exposed	3 / 17 (17.65%)			
occurrences (all)	5			
Asteatosis				
subjects affected / exposed	2 / 17 (11.76%)			
occurrences (all)	3			
Eczema				
subjects affected / exposed	2 / 17 (11.76%)			
occurrences (all)	3			
Urticaria				
subjects affected / exposed	2 / 17 (11.76%)			
occurrences (all)	2			
Dermatitis Allergic				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Dermatitis Atopic				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Dermatitis Diaper				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	2			
Dry Skin				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Hypertrophic Scar				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Miliaria				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Rash				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Skin Erosion				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			

Renal and urinary disorders Proteinuria subjects affected / exposed occurrences (all)	 1 / 17 (5.88%) 1		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Pharyngitis subjects affected / exposed occurrences (all) Conjunctivitis subjects affected / exposed occurrences (all) Otitis Media subjects affected / exposed occurrences (all) Gastroenteritis subjects affected / exposed occurrences (all) Hordeolum subjects affected / exposed occurrences (all) Impetigo subjects affected / exposed occurrences (all) Sinusitis subjects affected / exposed occurrences (all) Urinary Tract Infection subjects affected / exposed occurrences (all) Varicella subjects affected / exposed occurrences (all) Adenoviral Conjunctivitis	 9 / 17 (52.94%) 48 7 / 17 (41.18%) 17 5 / 17 (29.41%) 8 4 / 17 (23.53%) 4 2 / 17 (11.76%) 3 2 / 17 (11.76%) 3 2 / 17 (11.76%) 2 2 / 17 (11.76%) 2 2 / 17 (11.76%) 2 2 / 17 (11.76%) 2		

subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Adenovirus Infection				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Bronchiolitis				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Bronchitis				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Candida Infection				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Cellulitis				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Croup Infectious				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Dermatitis Infected				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Erythema Infectiosum				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Folliculitis				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Herpangina				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Molluscum Contagiosum				
subjects affected / exposed	1 / 17 (5.88%)			
occurrences (all)	1			
Mycoplasma Infection				

subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Paronychia subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 2		
Pneumonia subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Respiratory Syncytial Virus Infection subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Streptococcal Infection subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Upper Respiratory Tract Infection subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Metabolism and nutrition disorders Decreased Appetite subjects affected / exposed occurrences (all)	2 / 17 (11.76%) 3		
Dyslipidaemia subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Hyperlipidaemia subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Hypocarnitinaemia subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		
Hypokalaemia subjects affected / exposed occurrences (all)	1 / 17 (5.88%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported