Clinical trial results:
A Multicenter, Multinational, Open-Label Study of Anti-Laronidase Antibody Formation and Urinary GAG Levels in Patients with Mucopolysaccaridosis I (MPS I) Being Treated with Aldurazyme® (laronidase)

Summary

EudraCT number	2015-000585-61
Trial protocol	Outside EU/EEA
Global end of trial date	25 May 2007

Results information

Result version number	v1 (current)
This version publication date	01 April 2016
First version publication date	25 July 2015

Trial information

Trial identification

Sponsor protocol code	ALID02003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00144768
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Genzyme Corporation
Sponsor organisation address	500 Kendall Street, Cambridge, MA, United States, 02142
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?	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?	No

Global end of trial reached?	Yes
Global end of trial date	25 May 2007
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine whether the development of antibodies to laronidase in subjects with MPS I receiving Aldurazyme impairs the clearance of the glycosaminoglycan (GAG) substrate.

Protection of trial subjects:

Paediatric subjects: The study was conducted by investigators experienced in the treatment of pediatric subjects. 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.
Adult subject: Subjects were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the subject and considering the local culture. During the course of the trial, subjects were provided with individual subject cards indicating the nature of the trial the subject is participating, contact details and any information needed in the event of a medical emergency.
Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 July 2004
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	United States: 6
Worldwide total number of subjects	6
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)	1
Children (2-11 years)	4
Adolescents (12-17 years)	0
Adults (18-64 years)	1
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 3 sites in the United States of America between 20 July 2004 and 25 May 2007.

Pre-assignment

Screening details:

A total of 6 subjects were enrolled in the study.

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	Laronidase

Arm description:

Laronidase for 2.8 years.

Arm type	Experimental
Investigational medicinal product name	Laronidase
Investigational medicinal product code	
Other name	Aldurazyme ®
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Laronidase 0.58 mg/kg (100 U/kg) administered weekly.

Number of subjects in period 1	Laronidase
Started	6
Completed	0
Not completed	6
Consent withdrawn by subject	1
Adverse event	1
Unspecified	4

Baseline characteristics

Reporting groups	
Reporting group title	Laronidase
Reporting group description: Laronidase for 2.8 years.	

Reporting group values	Laronidase	Total	
Number of subjects	6	6	
Age categorical Units: Subjects			
Infants and toddlers (28 days-23 months)	1	1	
Children (2-11 years)	4	4	
Adults (18-64 years)	1	1	
Gender categorical Units: Subjects			
Female	3	3	
Male	3	3	

End points

End points reporting groups

Reporting group title	Laronidase
Reporting group description:	
Laronidase for 2.8 years.	

Primary: Percentage Change from Baseline in Urinary Glycosaminoglycan (GAG) Levels

End point title	Percentage Change from Baseline in Urinary Glycosaminoglycan (GAG) Levels[1]
End point description:	
Number of subjects analysed = all enrolled subjects who received at least one study infusion of Aldurazyme and data available for urinary GAG. Here, 'n' signifies the number of subjects with data available at the study time points.	
End point type	Primary
End point timeframe:	
Baseline, Week 26, 52	

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: Only descriptive data was planned for this outcome measure.

End point values	Laronidase			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: percent change				
median (full range (min-max))				
Week 26 (n=2)	-51.11 (-55.97 to -46.24)			
Week 52 (n=3)	-50 (-56.95 to -43.31)			

Statistical analyses

No statistical analyses for this end point

Primary: Immunogenicity

End point title	Immunogenicity[2]
End point description:	
End point type	Primary
End point timeframe:	
Up to Week 52	

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 this endpoint was not analysed, so no statistical analysis was provided.

End point values	Laronidase			
Subject group type	Reporting group			
Number of subjects analysed	0[3]			
Units: titre				
arithmetic mean (standard deviation)	()			

Notes:

[3] - Endpoint was not analysed due to insufficient data.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All Adverse Events (AE) were collected from signature of the informed consent form up to the final visit (up to 145 Weeks) regardless of seriousness or relationship to investigational product.

Adverse event reporting additional description:

Reported adverse events are treatment-emergent adverse events that is AEs that developed/worsened during the 'on treatment period' (from the first infusion of study drug upto last infusion of study drug). Analysis was performed on safety population included all enrolled subjects who received at least one infusion of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	10.1

Reporting groups

Reporting group title	Laronidase

Reporting group description:

Laronidase for 2.8 years.

Serious adverse events	Laronidase		
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 6 (83.33%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Collapse Of Lung			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Shunt Occlusion			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Congenital, familial and genetic disorders			
Foramen Magnum Stenosis			

subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cervical Myelopathy			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intracranial Pressure Increased			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Headache			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Local Swelling			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Drug Hypersensitivity			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Intestinal Obstruction			

subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Swollen Tongue				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Atelectasis				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cough				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Diaphragmatic Hernia				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Wheezing				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory Failure				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Skin and subcutaneous tissue disorders				

Swelling Face				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Idiopathic Urticaria				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urticaria				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Pain In Extremity				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sacroiliitis				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Bacterial Tracheitis				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Central Line Infection				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Lobar Pneumonia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteomyelitis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Staphylococcal Infection			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tracheitis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Laronidase		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)		
Vascular disorders			
Flushing			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Pallor			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
General disorders and administration site conditions			

Catheter Site Erythema subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 1			
Catheter Site Pain subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 1			
Chills subjects affected / exposed occurrences (all)	 2 / 6 (33.33%) 3			
Disease Progression subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 1			
Fatigue subjects affected / exposed occurrences (all)	 2 / 6 (33.33%) 2			
Infusion Site Swelling subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 1			
Injection Site Reaction subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 1			
Irritability subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 2			
Non-Cardiac Chest Pain subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 1			
Oedema Peripheral subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 1			
Pyrexia subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 3			
Reproductive system and breast disorders				

Testicular Pain			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Atelectasis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Choking			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Cough			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Diaphragmatic Hernia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	2		
Dyspnoea			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Hypoventilation			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Hypoxia			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Increased Upper Airway Secretion			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Lung Disorder			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Nasal Congestion			

subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Pharyngolaryngeal Pain			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Rhinitis Allergic			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Rhinorrhoea			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	3		
Throat Irritation			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	2		
Sleep Apnoea Syndrome			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Psychiatric disorders			
Abnormal Behaviour			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Agitation			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	2		
Restlessness			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Investigations			
Blood Iron Decreased			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Cardiac Murmur			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Blood Urine Present			

subjects affected / exposed occurrences (all) Coagulation Time Prolonged subjects affected / exposed occurrences (all) Oxygen Saturation Decreased subjects affected / exposed occurrences (all) Weight Decreased subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1 1 / 6 (16.67%) 1 1 / 6 (16.67%) 2 2 / 6 (33.33%) 3		
Injury, poisoning and procedural complications Incision Site Pain subjects affected / exposed occurrences (all) Procedural Nausea subjects affected / exposed occurrences (all) Shunt Occlusion subjects affected / exposed occurrences (all)	 3 / 6 (50.00%) 8 1 / 6 (16.67%) 1 1 / 6 (16.67%) 1		
Congenital, familial and genetic disorders Foramen Magnum Stenosis subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 1		
Cardiac disorders Cardiomegaly subjects affected / exposed occurrences (all) Cyanosis subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 1 1 / 6 (16.67%) 1		
Nervous system disorders Cervical Myelopathy subjects affected / exposed occurrences (all)	 2 / 6 (33.33%) 2		

Convulsion subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 2		
Headache subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 10		
Hyperreflexia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Hypoaesthesia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Intracranial Pressure Increased subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 2		
Neurological Symptom subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Spastic Paraplegia subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Unresponsive To Stimuli subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 3		
Ear and labyrinth disorders Conductive Deafness subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Hearing Impaired subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1		
Otorrhoea subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 2		
Eye disorders			

Cataract				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Conjunctivitis				
subjects affected / exposed	3 / 6 (50.00%)			
occurrences (all)	3			
Eye Discharge				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Eye Swelling				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	3			
Gastrointestinal disorders				
Abdominal Distension				
subjects affected / exposed	2 / 6 (33.33%)			
occurrences (all)	2			
Abdominal Pain				
subjects affected / exposed	3 / 6 (50.00%)			
occurrences (all)	3			
Diarrhoea				
subjects affected / exposed	3 / 6 (50.00%)			
occurrences (all)	5			
Dry Mouth				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Faecal Incontinence				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Gastrooesophageal Reflux Disease				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	2			
Gingivitis				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Haematochezia				

subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	4		
Reflux Oesophagitis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Umbilical Hernia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	5 / 6 (83.33%)		
occurrences (all)	10		
Hepatobiliary disorders			
Hepatosplenomegaly			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Dermatitis Contact			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Idiopathic Urticaria			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	2		
Erythema Multiforme			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Dermatitis Diaper			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	4		
Petechiae			

subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all) Pruritus Allergic subjects affected / exposed occurrences (all) Rash Generalised subjects affected / exposed occurrences (all) Urticaria subjects affected / exposed occurrences (all)	1 / 6 (16.67%) 1 2 / 6 (33.33%) 2 1 / 6 (16.67%) 1 1 / 6 (16.67%) 1 3 / 6 (50.00%) 34		
Renal and urinary disorders Dysuria subjects affected / exposed occurrences (all) Neurogenic Bladder subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 1 1 / 6 (16.67%) 1		
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all)	 1 / 6 (16.67%) 2		
Musculoskeletal and connective tissue disorders Back Pain subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all) Joint Contracture subjects affected / exposed occurrences (all) Kyphosis	 2 / 6 (33.33%) 2 1 / 6 (16.67%) 1 2 / 6 (33.33%) 2		

subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Muscle Atrophy			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Muscle Spasms			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Osteoporosis			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	2		
Pain In Extremity			
subjects affected / exposed	2 / 6 (33.33%)		
occurrences (all)	3		
Sacroiliitis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Infections and infestations			
Bacteraemia			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Cellulitis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Candida Nappy Rash			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Ear Infection			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Folliculitis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		
Incision Site Cellulitis			
subjects affected / exposed	1 / 6 (16.67%)		
occurrences (all)	1		

Gastroenteritis				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Influenza				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Nasopharyngitis				
subjects affected / exposed	2 / 6 (33.33%)			
occurrences (all)	4			
Otitis Externa				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Osteomyelitis				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Otitis Media				
subjects affected / exposed	2 / 6 (33.33%)			
occurrences (all)	5			
Otitis Media Acute				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Otitis Media Bacterial				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Otitis Media Chronic				
subjects affected / exposed	2 / 6 (33.33%)			
occurrences (all)	3			
Pneumonia				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	1			
Respiratory Tract Infection				
subjects affected / exposed	3 / 6 (50.00%)			
occurrences (all)	5			
Rhinitis				
subjects affected / exposed	1 / 6 (16.67%)			
occurrences (all)	2			

Sinusitis subjects affected / exposed occurrences (all) Tracheitis subjects affected / exposed occurrences (all) Upper Respiratory Tract Infection subjects affected / exposed occurrences (all) Viral Upper Respiratory Tract Infection subjects affected / exposed occurrences (all)	2 / 6 (33.33%) 4 1 / 6 (16.67%) 3 5 / 6 (83.33%) 10 2 / 6 (33.33%) 2		
Metabolism and nutrition disorders Dehydration subjects affected / exposed occurrences (all)	2 / 6 (33.33%) 3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
13 January 2004	Amendment included follwoing statements: Text was added to clarify that testing for immunoglobulin G (IgG) antibodies would be performed at baseline in addition to quarterly during the study. Repeat testing of urinary GAG levels was changed from quarterly to within 1 month after any urinary GAG value that was >= 15% higher than a previous value. The criterion exempting subjects from neutralizing antibody testing if they had undergone a recent surgical procedure was removed. Text was added to clarify collection of urine samples for urinary GAG measurement.
17 February 2005	-The number of subjects to be enrolled was reduced from 50 to 25, due to a lower than anticipated subjects accrual rate. -The criterion for testing neutralizing antibodies at Week 12 was clarified as being done if the value was <35% of the baseline value. -The window for baseline urinary GAG, safety laboratory, urinalysis, and IgG evaluations for subjects <5 years of age were shortened to within 3 months prior to enrollment.
28 December 2005	The purpose of this amendment was to clarify sample collection procedures for subjects who had been treated with Aldurazyme prior to study entry. Wording was added to state that testing of neutralizing antibodies in subjects who did not enter the study as treatment naïve could be achieved by using archived samples taken prior to study entry, if available.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported