Clinical trial results:
A Phase 4, Multi-Center, Multi-National, Open-Label, Randomized, Two Dose Level Study of Naglazyme® (galsulfase) in Infants with Maroteaux-Lamy Syndrome (MPS VI)

Summary

EudraCT number	2005-003512-30
Trial protocol	FR PT
Global end of trial date	30 April 2009

Results information

Result version number	v1 (current)
This version publication date	18 December 2019
First version publication date	18 December 2019

Trial information

Trial identification

Sponsor protocol code	ASB-008

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00299000
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	BioMarin Pharmaceutical Inc.
Sponsor organisation address	105 Digital Drive, Novato, United States, CA 94949
Public contact	Clinical Trials Information, BioMarin Pharmaceutical Inc., clinicaltrials@bmrn.com
Scientific contact	Clinical Trials Information, BioMarin Pharmaceutical Inc., 800 983-4587, medinfo@bmrn.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	14 January 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 April 2009
Global end of trial reached?	Yes
Global end of trial date	30 April 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to evaluate the efficacy of two dose levels of Naglazyme in preventing the progression of skeletal dysplasia in infants under the age of one year who have MPS VI by monitoring physical appearance, x-ray of the skeletal system and growth.

Protection of trial subjects:

This clinical study was designed, conducted, recorded, and reported in compliance with the principles of Good Clinical Practice (GCP) guidelines. These guidelines are stated in U.S. federal regulations as well as "Guidance for Good Clinical Practice," International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use.

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	08 May 2006
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 2
Country: Number of subjects enrolled	Portugal: 1
Country: Number of subjects enrolled	France: 1
Worldwide total number of subjects	4
EEA total number of subjects	2

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)	4
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:

This study was conducted at 3 primary study centers.

Pre-assignment

Screening details:

Subjects enrolled were 4 and all subjects completed the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Naglazyme, 1.0 mg/kg

Arm description:

Weekly infusions for minimum of 52 weeks

Arm type	Experimental
Investigational medicinal product name	Naglazyme, 1.0 mg/kg
Investigational medicinal product code	
Other name	Recombinant human N-acetylgalactosamine 4-sulfatase, rh-arylsulfatase B, rhASB
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Naglazyme, 1.0 mg/kg/week was administered as an intravenous infusion over no less than a 4-hour period per infusion for minimum of 52 weeks. Naglazyme is diluted in sterile 0.9% sodium chloride solution

Arm title	Naglazyme, 2.0 mg/kg

Arm description:

Weekly infusions for minimum of 52 weeks

Arm type	Experimental
Investigational medicinal product name	Naglazyme, 2.0 mg/kg
Investigational medicinal product code	
Other name	Recombinant human N-acetylgalactosamine 4-sulfatase, rh-arylsulfatase B, rhASB
Pharmaceutical forms	Injection
Routes of administration	Intravenous use

Dosage and administration details:

Naglazyme, 2.0 mg/kg/week was administered as an intravenous infusion over no less than a 4-hour period per infusion for minimum of 52 weeks. Naglazyme is diluted in sterile 0.9% sodium chloride solution

Number of subjects in period 1	Naglazyme, 1.0 mg/kg	Naglazyme, 2.0 mg/kg
Started	2	2
Completed	2	2

Baseline characteristics

Reporting groups	
Reporting group title	Naglazyme, 1.0 mg/kg
Reporting group description:	
Weekly infusions for minimum of 52 weeks	
Reporting group title	Naglazyme, 2.0 mg/kg
Reporting group description:	
Weekly infusions for minimum of 52 weeks	

Reporting group values	Naglazyme, 1.0 mg/kg	Naglazyme, 2.0 mg/kg	Total
Number of subjects	2	2	4
Age categorical Units: Subjects			
Infants and toddlers (28 days-23 months)	2	2	4
Age continuous Units: months			
arithmetic mean	6.05	12.4	
standard deviation	± 3.89	± 0.42	-
Gender categorical Units: Subjects			
Female	0	0	0
Male	2	2	4

End points

End points reporting groups

Reporting group title	Naglazyme, 1.0 mg/kg
Reporting group description:	
Weekly infusions for minimum of 52 weeks	
Reporting group title	Naglazyme, 2.0 mg/kg
Reporting group description:	
Weekly infusions for minimum of 52 weeks	

Primary: Change in Height

End point title	Change in Height[1]
End point description:	

End point type	Primary
End point timeframe:	
52 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: Statistical testing was conducted, but no formal statistical inference was planned for the study because of the small number of subjects planned to enroll into the study.

End point values	Naglazyme, 1.0 mg/kg	Naglazyme, 2.0 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	2		
Units: centimeters				
arithmetic mean (standard deviation)				
Height at Baseline	67.3 (± 5.1)	80.3 (± 1.8)		
Height at week 52	81.9 (± 1.8)	91.3 (± 5.2)		
Change in Height	14.6 (± 6.9)	11.0 (± 7.0)		

Statistical analyses

No statistical analyses for this end point

Primary: Change in Weight

End point title	Change in Weight[2]
End point description:	

End point type	Primary
End point timeframe:	
52 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: Statistical testing was conducted, but no formal statistical inference was planned for the study because of the small number of subjects planned to enroll into the study.

End point values	Naglazyme, 1.0 mg/kg	Naglazyme, 2.0 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	2		
Units: Kilograms				
arithmetic mean (standard deviation)				
Weight at Baseline	7.1 (± 0.3)	10.2 (± 0.6)		
Weight at week 52	11.3 (± 0.3)	13.3 (± 1.0)		
Change in weight	4.2 (± 0.6)	3.1 (± 1.6)		

Statistical analyses

No statistical analyses for this end point

Primary: Change in Head Circumference

End point title	Change in Head Circumference[3]

End point description:

End point type	Primary

End point timeframe:

52 weeks

Notes:

[3] - 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: Statistical testing was conducted, but no formal statistical inference was planned for the study because of the small number of subjects planned to enroll into the study.

End point values	Naglazyme, 1.0 mg/kg	Naglazyme, 2.0 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	2		
Units: Centimeter				
arithmetic mean (standard deviation)				
Head circumference at Baseline	43.5 (± 3.0)	49.1 (± 0.5)		
Head circumference at 52 weeks	48.5 (± 1.0)	51.8 (± 0.8)		
Change in Head circumference	5.0 (± 4.0)	2.7 (± 1.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in Urinary Glycosaminoglycan Levels

End point title	Change in Urinary Glycosaminoglycan Levels

End point description:

Change in urinary GAG levels was calculated from baseline to week 52 of treatment

End point type	Secondary

End point timeframe:

52 weeks

End point values	Naglazyme, 1.0 mg/kg	Naglazyme, 2.0 mg/kg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	2		
Units: ug/mg				
arithmetic mean (standard deviation)				
Baseline	1041.87 (± 86.32)	698.95 (± 142.34)		
Week 52	261.15 (± 54.38)	178.10 (± 42.43)		
Change from Baseline to Week 52	-780.72 (± 140.69)	-520.85 (± 99.91)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All patients received weekly infusions of Nagalzyme for a minimum of 52 weeks. The range in time of exposure to Naglazyme for the duration of the study was 52.9 to 153.30 weeks

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.0

Reporting groups

Reporting group title	Naglazyme, 1.0 mg/kg
Reporting group description: -	
Reporting group title	Naglazyme, 2.0 mg/kg

Reporting group description: -

Serious adverse events	Naglazyme, 1.0 mg/kg	Naglazyme, 2.0 mg/kg	
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)	2 / 2 (100.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Vascular disorders			
Poor venous access			
subjects affected / exposed	1 / 2 (50.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Cast application			
subjects affected / exposed	0 / 2 (0.00%)	1 / 2 (50.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Febrile convulsion			
subjects affected / exposed	0 / 2 (0.00%)	1 / 2 (50.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Umbilical hernia			

subjects affected / exposed	0 / 2 (0.00%)	1 / 2 (50.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Adenoidal hypertrophy			
subjects affected / exposed	0 / 2 (0.00%)	1 / 2 (50.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	1 / 2 (50.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Scoliosis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 2 (50.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	1 / 2 (50.00%)	0 / 2 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	0 / 2 (0.00%)	1 / 2 (50.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Naglazyme, 1.0 mg/kg	Naglazyme, 2.0 mg/kg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 2 (100.00%)	2 / 2 (100.00%)	
General disorders and administration site conditions			

Pyrexia			
subjects affected / exposed	2 / 2 (100.00%)	1 / 2 (50.00%)	
occurrences (all)	8	31	
Gastrointestinal disorders			
Diarrhea			
subjects affected / exposed	2 / 2 (100.00%)	2 / 2 (100.00%)	
occurrences (all)	4	3	
Umbilical hernia			
subjects affected / exposed	2 / 2 (100.00%)	1 / 2 (50.00%)	
occurrences (all)	3	1	
Vomiting			
subjects affected / exposed	1 / 2 (50.00%)	2 / 2 (100.00%)	
occurrences (all)	2	3	
Respiratory, thoracic and mediastinal disorders			
Nasal congestion			
subjects affected / exposed	2 / 2 (100.00%)	1 / 2 (50.00%)	
occurrences (all)	15	1	
Infections and infestations			
Ear infection			
subjects affected / exposed	2 / 2 (100.00%)	2 / 2 (100.00%)	
occurrences (all)	2	4	
Rhinitis			
subjects affected / exposed	1 / 2 (50.00%)	2 / 2 (100.00%)	
occurrences (all)	3	3	
Upper respiratory tract infections			
subjects affected / exposed	2 / 2 (100.00%)	1 / 2 (50.00%)	
occurrences (all)	9	3	

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