



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