



Clinical trial results:

A Randomized, Double-Blind, Pilot Study of the Safety and Physiological Effects of Two Doses of BMN 110 in Patients with Mucopolysaccharidosis IVA (Morquio A Syndrome)

Summary

| | |
|--------------------------|------------------|
| EudraCT number | 2011-005682-20 |
| Trial protocol | DE GB |
| Global end of trial date | 20 November 2014 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 06 December 2017 |
| First version publication date | 06 December 2017 |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | MOR-008 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01609062 |
| 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., clinicaltrials@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? | No |

Notes:

Results analysis stage

| | |
|------------------------------------------------------|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 05 March 2015 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 20 November 2014 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

- To evaluate the safety of 2.0 and 4.0 mg/kg/week BMN 110 administered for 27 weeks

The primary objective for extending the Phase 2 study is:

- To evaluate the long-term safety of 2.0 and 4.0 mg/kg/week BMN 110 in patients with MPS IVA

Protection of trial subjects:

The study was conducted in accordance with the principles of the Declaration of Helsinki including amendments in force up to and including the time the study was conducted. The study was conducted in compliance with the International Conference on Harmonisation E6 Guideline for Good Clinical Practice, and is compliant with the European Union Clinical Trial Directive 2001/20/EC. The study was also conducted in compliance with the United Federal Regulations.

Background therapy: -

Evidence for comparator: -

| | |
|-----------------------------------------------------------|-------------|
| Actual start date of recruitment | 15 May 2012 |
| 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 | Canada: 6 |
| Country: Number of subjects enrolled | Germany: 3 |
| Country: Number of subjects enrolled | United Kingdom: 2 |
| Country: Number of subjects enrolled | United States: 14 |
| Worldwide total number of subjects | 25 |
| EEA total number of subjects | 5 |

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) | 0 |

| | |
|---------------------------|----|
| Children (2-11 years) | 14 |
| Adolescents (12-17 years) | 8 |
| Adults (18-64 years) | 3 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

After providing Informed Consent, subjects were screened for eligibility over a 3-week period.

Period 1

| | |
|------------------------------|----------------------------------------------|
| Period 1 title | Primary Phase |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst |

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|------------------|-----------------------|
| Arm title | BMN110 2.0 mg/kg/week |
|------------------|-----------------------|

Arm description: -

| | |
|----------------------------------------|--------------------------------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Elosulfase alfa |
| Investigational medicinal product code | BMN110 |
| Other name | Vimizim, recombinant human N-acetylgalactosamine-6-sulfatase |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Weekly IV infusions of BMN 110 2.0 mg/kg/week for 27 consecutive weeks (Week 0 through Week 26). Each infusion was administered over a period of approximately 4 hours.

| | |
|------------------|-----------------------|
| Arm title | BMN110 4.0 mg/kg/week |
|------------------|-----------------------|

Arm description: -

| | |
|----------------------------------------|--------------------------------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Elosulfase alfa |
| Investigational medicinal product code | BMN110 |
| Other name | Vimizim, recombinant human N-acetylgalactosamine-6-sulfatase |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Weekly IV infusions of BMN 110 4.0 mg/kg/week for 27 consecutive weeks (Week 0 through Week 26). Each infusion was administered over a period of approximately 4 hours.

| Number of subjects in period 1 | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week |
|--------------------------------|-----------------------|-----------------------|
| Started | 15 | 10 |
| Completed | 15 | 10 |

| | |
|------------------------------|----------------------------------------------|
| Period 2 | |
| Period 2 title | Extension Phase |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Double blind |
| Roles blinded | Subject, Investigator, Monitor, Data analyst |

Arms

| | |
|------------------------------|-----------------------|
| Are arms mutually exclusive? | Yes |
| Arm title | BMN110 2.0 mg/kg/week |

Arm description: -

| | |
|----------------------------------------|--------------------------------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Elosulfase alfa |
| Investigational medicinal product code | BMN110 |
| Other name | Vimizim, recombinant human N-acetylgalactosamine-6-sulfatase |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Weekly IV infusions of BMN 110 2.0 mg/kg/week for 27 consecutive weeks (Week 0 through Week 26). Each infusion was administered over a period of approximately 4 hours.

| | |
|------------------|-----------------------|
| Arm title | BMN110 4.0 mg/kg/week |
|------------------|-----------------------|

Arm description: -

| | |
|----------------------------------------|--------------------------------------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Elosulfase alfa |
| Investigational medicinal product code | BMN110 |
| Other name | Vimizim, recombinant human N-acetylgalactosamine-6-sulfatase |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Weekly IV infusions of BMN 110 4.0 mg/kg/week for 27 consecutive weeks (Week 0 through Week 26). Each infusion was administered over a period of approximately 4 hours.

| Number of subjects in period 2 | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week |
|---------------------------------------|------------------------------|------------------------------|
| Started | 15 | 10 |
| Completed | 0 | 0 |
| Not completed | 15 | 10 |
| Anticipated Surgery | - | 1 |
| Pregnancy | 1 | - |
| Study Terminated by Sponsor | 14 | 9 |

Baseline characteristics

Reporting groups

| | |
|--------------------------------|-----------------------|
| Reporting group title | BMN110 2.0 mg/kg/week |
| Reporting group description: - | |
| Reporting group title | BMN110 4.0 mg/kg/week |
| Reporting group description: - | |

| Reporting group values | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week | Total |
|------------------------------------------------------------------------------|-----------------------|-----------------------|-------|
| Number of subjects | 15 | 10 | 25 |
| Age categorical Units: Subjects | | | |
| 7 - 11 | 9 | 5 | 14 |
| 12 - 18 | 3 | 5 | 8 |
| >= 19 | 3 | 0 | 3 |
| Age continuous Units: Years | | | |
| arithmetic mean | 14.9 | 12 | - |
| standard deviation | ± 9.32 | ± 3.16 | - |
| Gender categorical Units: Subjects | | | |
| Female | 12 | 4 | 16 |
| Male | 3 | 6 | 9 |
| Distance Walked in Six Minutes Units: meters | | | |
| arithmetic mean | 369.6 | 376.3 | - |
| standard deviation | ± 89.19 | ± 69.98 | - |
| Three Minute Stair Climb Rate Units: steps/minute | | | |
| arithmetic mean | 65.5 | 64.2 | - |
| standard deviation | ± 21.42 | ± 23.32 | - |
| Normalized Urine Keratan Sulfate Units: ug/mg | | | |
| arithmetic mean | 16.4 | 18.8 | - |
| standard deviation | ± 15.23 | ± 9.03 | - |
| Respiratory Function Test MVV Units: L/min | | | |
| arithmetic mean | 42.2 | 57.2 | - |
| standard deviation | ± 22.81 | ± 33.83 | - |
| Respiratory Function Test FVC Units: Liter | | | |
| arithmetic mean | 1.9 | 1.8 | - |
| standard deviation | ± 1.21 | ± 1.15 | - |
| Cardiopulmonary Exercise Testing (CPET) - Duration of Exercise Units: min | | | |
| arithmetic mean | 8 | 7.1 | - |
| standard deviation | ± 2.63 | ± 1.42 | - |
| Cardiopulmonary Exercise Testing | | | |

| | | | |
|-------------------------------------------------------------------------------------------------------------------------|-------------------|------------------|---|
| (CPET) - Peak Workload Units: Watts arithmetic mean standard deviation | 43.5 ± 29.88 | 35.8 ± 17.2 | - |
| Cardiopulmonary Exercise Testing (CPET) - O2 Pulse Units: VE/VCO2 arithmetic mean standard deviation | 4.9 ± 2.63 | 4.7 ± 1.06 | - |
| Cardiopulmonary Exercise Testing (CPET) - Aerobic Efficiency Units: mL/watt arithmetic mean standard deviation | 12.8 ± 3.87 | 14.1 ± 1.47 | - |
| Cardiopulmonary Exercise Testing (CPET) - Peak VO2 Units: mL/min arithmetic mean standard deviation | 848.3 ± 487.45 | 724.6 ± 220.7 | - |
| Muscle Strength Testing - Knee Extension Test Units: N*m arithmetic mean standard deviation | 31.6 ± 16.97 | 23.9 ± 22.29 | - |
| Muscle Strength Testing - Knee Flexion Test Units: N*m arithmetic mean standard deviation | 20.2 ± 15.07 | 18.9 ± 14.51 | - |
| Muscle Strength Testing - Elbow Flexion Test Units: N*m arithmetic mean standard deviation | 9.6 ± 7.61 | 12.3 ± 10.94 | - |

Subject analysis sets

| | |
|----------------------------|-----------------------------|
| Subject analysis set title | Modified Intent-to-Treat |
| Subject analysis set type | Modified intention-to-treat |

Subject analysis set description:

All subjects who were randomized to study treatment, received at least one dose of study drug, and had at least one post-treatment observation. The primary efficacy analyses for all efficacy endpoints were based on the modified ITT population and data were analyzed according to the treatment assigned at randomization.

| | |
|----------------------------|-------------------|
| Subject analysis set title | Safety Population |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

All subjects who received one or more doses of study drug

| Reporting group values | Modified Intent-to-Treat | Safety Population | |
|------------------------------------|--------------------------|-------------------|--|
| Number of subjects | 25 | 25 | |
| Age categorical Units: Subjects | | | |
| 7 - 11 | 14 | 14 | |

| | | | |
|---------|---|---|--|
| 12 - 18 | 8 | 8 | |
| >= 19 | 3 | 3 | |

| | | | |
|-------------------------------------------------------------------------------------------------------------------------|------------------|------------------|--|
| Age continuous Units: Years arithmetic mean standard deviation | 13.7 ± 7.52 | 13.7 ± 7.52 | |
| Gender categorical Units: Subjects | | | |
| Female | 16 | 16 | |
| Male | 9 | 9 | |
| Distance Walked in Six Minutes Units: meters arithmetic mean standard deviation | 372.2 ± 80.55 | 372.2 ± 80.55 | |
| Three Minute Stair Climb Rate Units: steps/minute arithmetic mean standard deviation | 65 ± 21.73 | 65 ± 21.73 | |
| Normalized Urine Keratan Sulfate Units: ug/mg arithmetic mean standard deviation | 17.4 ± 12.96 | 17.4 ± 12.96 | |
| Respiratory Function Test MVV Units: L/min arithmetic mean standard deviation | 49 ± 28.65 | 49 ± 28.65 | |
| Respiratory Function Test FVC Units: Liter arithmetic mean standard deviation | 1.9 ± 1.16 | 1.9 ± 1.16 | |
| Cardiopulmonary Exercise Testing (CPET) - Duration of Exercise Units: min arithmetic mean standard deviation | 7.7 ± 2.29 | 7.7 ± 2.29 | |
| Cardiopulmonary Exercise Testing (CPET) - Peak Workload Units: Watts arithmetic mean standard deviation | 40.9 ± 25.94 | 40.9 ± 25.94 | |
| Cardiopulmonary Exercise Testing (CPET) - O2 Pulse Units: VE/VCO2 arithmetic mean standard deviation | 4.9 ± 2.18 | 4.9 ± 2.18 | |
| Cardiopulmonary Exercise Testing (CPET) - Aerobic Efficiency Units: mL/watt arithmetic mean standard deviation | 13.3 ± 3.21 | 13.3 ± 3.21 | |
| Cardiopulmonary Exercise Testing (CPET) - Peak VO2 | | | |

| | | | |
|------------------------------------------------------------------------------------------------------|------------------|------------------|--|
| Units: mL/min arithmetic mean standard deviation | 807.1 ± 412.6 | 807.1 ± 412.6 | |
| Muscle Strength Testing - Knee Extension Test Units: N*m arithmetic mean standard deviation | 28.5 ± 19.22 | 28.5 ± 19.22 | |
| Muscle Strength Testing - Knee Flexion Test Units: N*m arithmetic mean standard deviation | 19.7 ± 14.55 | 19.7 ± 14.55 | |
| Muscle Strength Testing - Elbow Flexion Test Units: N*m arithmetic mean standard deviation | 10.6 ± 8.86 | 10.6 ± 8.86 | |

End points

End points reporting groups

| | |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------|
| Reporting group title | BMN110 2.0 mg/kg/week |
| Reporting group description: - | |
| Reporting group title | BMN110 4.0 mg/kg/week |
| Reporting group description: - | |
| Reporting group title | BMN110 2.0 mg/kg/week |
| Reporting group description: - | |
| Reporting group title | BMN110 4.0 mg/kg/week |
| Reporting group description: - | |
| Subject analysis set title | Modified Intent-to-Treat |
| Subject analysis set type | Modified intention-to-treat |
| Subject analysis set description: All subjects who were randomized to study treatment, received at least one dose of study drug, and had at least one post-treatment observation. The primary efficacy analyses for all efficacy endpoints were based on the modified ITT population and data were analyzed according to the treatment assigned at randomization. | |
| Subject analysis set title | Safety Population |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: All subjects who received one or more doses of study drug | |

Primary: Serious Adverse Events

| | |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------|
| End point title | Serious Adverse Events ^[1] |
| End point description: No statistical analysis performed for this endpoint as it is descriptive analysis | |
| End point type | Primary |
| End point timeframe: Entire Study Period, up to 192 weeks or ETV (early termination visit) | |
| 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: No statistical analysis performed for this endpoint as it is descriptive analysis | |

| End point values | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week | Safety Population | |
|-----------------------------|-----------------------|-----------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 15 | 10 | 25 | |
| Units: Subjects | 3 | 2 | 5 | |

Statistical analyses

No statistical analyses for this end point

Primary: Non Serious Adverse Events

| | |
|-------------------------------------------------------------------------------------------------------------|-------------------------------------------|
| End point title | Non Serious Adverse Events ^[2] |
| End point description: No statistical analysis performed for this endpoint as it is descriptive analysis | |

| | |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|
| End point type | Primary |
| End point timeframe: | |
| Entire Study Period, up to 192 weeks or ETV (early termination visit) | |
| 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: No statistical analysis performed for this endpoint as it is descriptive analysis | |

| End point values | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week | Safety Population | |
|-----------------------------|-----------------------|-----------------------|----------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 15 | 10 | 25 | |
| Units: Subjects | 15 | 10 | 25 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 12 in Distance Walked in Six Minutes - Modified ITT Population

| | |
|------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Change from Baseline to Week 12 in Distance Walked in Six Minutes - Modified ITT Population |
| End point description: | Change from baseline in metres in 6-minute Walk Test. As a measure of endurance, a 6-minute walk test (6MWT) was performed according to the American Thoracic Society Guidelines. Patients were instructed to walk as far as possible in 6 minutes. |
| End point type | Secondary |
| End point timeframe: | |
| Baseline to Week 12 | |

| End point values | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week | Modified Intent-to-Treat | |
|--------------------------------------|-----------------------|-----------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 15 | 10 | 25 | |
| Units: metres | | | | |
| arithmetic mean (standard deviation) | 14.7 (± 30.9) | -8.9 (± 83.52) | 5.3 (± 57.55) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 24 in Distance Walked in Six Minutes - Modified ITT Population

| | |
|-----------------|---------------------------------------------------------------------------------------------|
| End point title | Change from Baseline to Week 24 in Distance Walked in Six Minutes - Modified ITT Population |
|-----------------|---------------------------------------------------------------------------------------------|

End point description:

Change from baseline in metres in 6-minute Walk Test. As a measure of endurance, a 6-minute walk test (6MWT) was performed according to the American Thoracic Society Guidelines. Patients were instructed to walk as far as possible in 6 minutes.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 24

| End point values | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week | Modified Intent-to-Treat | |
|--------------------------------------|-----------------------|-----------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 15 | 10 | 25 | |
| Units: metres | | | | |
| arithmetic mean (standard deviation) | -13 (\pm 54.12) | 0.1 (\pm 34.7) | -7.8 (\pm 46.94) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 52 in Distance Walked in Six Minutes - Modified ITT Population

| | |
|-----------------|---------------------------------------------------------------------------------------------|
| End point title | Change from Baseline to Week 52 in Distance Walked in Six Minutes - Modified ITT Population |
|-----------------|---------------------------------------------------------------------------------------------|

End point description:

Change from baseline in metres in 6-minute Walk Test. As a measure of endurance, a 6-minute walk test (6MWT) was performed according to the American Thoracic Society Guidelines. Patients were instructed to walk as far as possible in 6 minutes.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 52

| End point values | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week | Modified Intent-to-Treat | |
|--------------------------------------|-----------------------|-----------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 14 | 10 | 24 | |
| Units: metres | | | | |
| arithmetic mean (standard deviation) | 9 (\pm 48.41) | 31.8 (\pm 54.56) | 18.5 (\pm 51.19) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 12 in Average Three Minute Stair Climb

Rate - Modified ITT Population

| | |
|-----------------|----------------------------------------------------------------------------------------------------|
| End point title | Change from Baseline to Week 12 in Average Three Minute Stair Climb Rate - Modified ITT Population |
|-----------------|----------------------------------------------------------------------------------------------------|

End point description:

Change from baseline in the 3-minute Stair Climb Test (3MSCT). Patients walked up stairs that have a railing, which could be used for support, for 3 minutes, with the number of stairs climbed recorded. The test result was the number of steps climbed per minute.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 12

| End point values | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week | Modified Intent-to-Treat | |
|--------------------------------------|-----------------------|-----------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 15 | 10 | 25 | |
| Units: stairs/min | | | | |
| arithmetic mean (standard deviation) | -3.7 (± 13.16) | 1.7 (± 11.28) | -1.5 (± 12.49) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 24 in Average Three Minute Stair Climb Rate - Modified ITT Population

| | |
|-----------------|----------------------------------------------------------------------------------------------------|
| End point title | Change from Baseline to Week 24 in Average Three Minute Stair Climb Rate - Modified ITT Population |
|-----------------|----------------------------------------------------------------------------------------------------|

End point description:

Change from baseline in the 3-minute Stair Climb Test (3MSCT). Patients walked up stairs that have a railing, which could be used for support, for 3 minutes, with the number of stairs climbed recorded. The test result was the number of steps climbed per minute.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 24

| End point values | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week | Modified Intent-to-Treat | |
|--------------------------------------|-----------------------|-----------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 14 | 10 | 24 | |
| Units: stairs/min | | | | |
| arithmetic mean (standard deviation) | -2.2 (± 11.01) | 12.5 (± 15.26) | 3.9 (± 14.65) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 52 in Average Three Minute Stair Climb Rate - Modified ITT Population

| | |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------|
| End point title | Change from Baseline to Week 52 in Average Three Minute Stair Climb Rate - Modified ITT Population |
| End point description: Change from baseline in the 3-minute Stair Climb Test (3MSCT). Patients walked up stairs that have a railing, which could be used for support, for 3 minutes, with the number of stairs climbed recorded. The test result was the number of steps climbed per minute. | |
| End point type | Secondary |
| End point timeframe: Baseline to Week 52 | |

| End point values | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week | Modified Intent-to-Treat | |
|--------------------------------------|-----------------------|-----------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 15 | 10 | 25 | |
| Units: stairs/min | | | | |
| arithmetic mean (standard deviation) | -4.4 (\pm 9.82) | 10 (\pm 16.88) | 1.3 (\pm 14.66) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline to Week 12 in Respiratory Function Test MVV - Modified ITT Population

| | |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------|
| End point title | Percent Change From Baseline to Week 12 in Respiratory Function Test MVV - Modified ITT Population |
| End point description: Respiratory Function was assessed by spirometry in accordance with American Thoracic Society standards. Percent Change from Baseline in Maximum Voluntary Ventilation (MVV). | |
| End point type | Secondary |
| End point timeframe: Baseline to Week 12 | |

| End point values | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week | Modified Intent-to-Treat | |
|--------------------------------------|-----------------------|-----------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 12 | 10 | 22 | |
| Units: % change | | | | |
| arithmetic mean (standard deviation) | 12.8 (\pm 21.77) | 32.4 (\pm 140.73) | 21.7 (\pm 94) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline to Week 24 in Respiratory Function Test MVV - Modified ITT Population

| | |
|-----------------|----------------------------------------------------------------------------------------------------|
| End point title | Percent Change From Baseline to Week 24 in Respiratory Function Test MVV - Modified ITT Population |
|-----------------|----------------------------------------------------------------------------------------------------|

End point description:

Respiratory Function was assessed by spirometry in accordance with American Thoracic Society standards.

Percent Change from Baseline in Maximum Voluntary Ventilation (MVV).

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 24

| End point values | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week | Modified Intent-to-Treat | |
|--------------------------------------|-----------------------|-----------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 11 | 10 | 21 | |
| Units: % change | | | | |
| arithmetic mean (standard deviation) | 8.8 (± 17.2) | -0.6 (± 27) | 4.3 (± 22.34) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline to Week 52 in Respiratory Function Test MVV - Modified ITT Population

| | |
|-----------------|----------------------------------------------------------------------------------------------------|
| End point title | Percent Change From Baseline to Week 52 in Respiratory Function Test MVV - Modified ITT Population |
|-----------------|----------------------------------------------------------------------------------------------------|

End point description:

Respiratory Function was assessed by spirometry in accordance with American Thoracic Society standards.

Percent Change from Baseline in Maximum Voluntary Ventilation (MVV).

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 52

| End point values | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week | Modified Intent-to-Treat | |
|--------------------------------------|-----------------------|-----------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 12 | 10 | 22 | |
| Units: % change | | | | |
| arithmetic mean (standard deviation) | 2.2 (± 41.24) | -17.8 (± 38.61) | -6.9 (± 40.43) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline to Week 12 in Respiratory Function Test FVC - Modified ITT Population

| | |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------|
| End point title | Percent Change From Baseline to Week 12 in Respiratory Function Test FVC - Modified ITT Population |
| End point description: Respiratory Function was assessed by spirometry in accordance with American Thoracic Society standards. Percent Change from Baseline in Maximum Voluntary Ventilation (MVV). | |
| End point type | Secondary |
| End point timeframe: Baseline to Week 12 | |

| End point values | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week | Modified Intent-to-Treat | |
|--------------------------------------|-----------------------|-----------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 14 | 10 | 24 | |
| Units: % change | | | | |
| arithmetic mean (standard deviation) | 1.7 (± 8.77) | 3.2 (± 10.63) | 2.3 (± 9.39) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline to Week 24 in Respiratory Function Test FVC - Modified ITT Population

| | |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------|
| End point title | Percent Change From Baseline to Week 24 in Respiratory Function Test FVC - Modified ITT Population |
| End point description: Respiratory Function was assessed by spirometry in accordance with American Thoracic Society standards. Percent Change from Baseline in Forced Vital Capacity (FVC). | |
| End point type | Secondary |
| End point timeframe: Baseline to Week 24 | |

| End point values | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week | Modified Intent-to-Treat | |
|--------------------------------------|-----------------------|-----------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 14 | 10 | 24 | |
| Units: % change | | | | |
| arithmetic mean (standard deviation) | 3.4 (± 9.01) | 13 (± 16.3) | 7.4 (± 13.16) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change From Baseline to Week 52 in Respiratory Function Test FVC - Modified ITT Population

| | |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------|
| End point title | Percent Change From Baseline to Week 52 in Respiratory Function Test FVC - Modified ITT Population |
| End point description: Respiratory Function was assessed by spirometry in accordance with American Thoracic Society standards. Percent Change from Baseline in Forced Vital Capacity (FVC). | |
| End point type | Secondary |
| End point timeframe: Baseline to Week 52 | |

| End point values | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week | Modified Intent-to-Treat | |
|--------------------------------------|-----------------------|-----------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 15 | 10 | 25 | |
| Units: % change | | | | |
| arithmetic mean (standard deviation) | 4.8 (± 12.68) | 15.1 (± 15.94) | 8.9 (± 14.69) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline to Week 12 in Normalized Urine Keratan Sulfate - Modified ITT Population

| | |
|--------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------|
| End point title | Percent Change from Baseline to Week 12 in Normalized Urine Keratan Sulfate - Modified ITT Population |
| End point description: Urinary KS was measured by a quantitative method and normalized using the sample urinary creatinine measurement. | |
| End point type | Secondary |

End point timeframe:

Baseline to Week 12

| End point values | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week | Modified Intent-to-Treat | |
|--------------------------------------|-----------------------|-----------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 14 | 9 | 23 | |
| Units: % change | | | | |
| arithmetic mean (standard deviation) | -27.6 (± 25.1) | -50.9 (± 14) | -36.7 (± 24.07) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline to Week 24 in Normalized Urine Keratan Sulfate - Modified ITT Population

| | |
|-----------------|-------------------------------------------------------------------------------------------------------|
| End point title | Percent Change from Baseline to Week 24 in Normalized Urine Keratan Sulfate - Modified ITT Population |
|-----------------|-------------------------------------------------------------------------------------------------------|

End point description:

Urinary KS was measured by a quantitative method and normalized using the sample urinary creatinine measurement.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 24

| End point values | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week | Modified Intent-to-Treat | |
|--------------------------------------|-----------------------|-----------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 14 | 9 | 23 | |
| Units: % change | | | | |
| arithmetic mean (standard deviation) | -37.4 (± 23.21) | -55.5 (± 12.62) | -44.5 (± 21.39) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline to Week 52 in Normalized Urine Keratan Sulfate - Modified ITT Population

| | |
|-----------------|-------------------------------------------------------------------------------------------------------|
| End point title | Percent Change from Baseline to Week 52 in Normalized Urine Keratan Sulfate - Modified ITT Population |
|-----------------|-------------------------------------------------------------------------------------------------------|

End point description:

Urinary KS was measured by a quantitative method and normalized using the sample urinary creatinine measurement.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 52

| End point values | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week | Modified Intent-to-Treat | |
|--------------------------------------|-----------------------|-----------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 10 | 5 | 15 | |
| Units: % change | | | | |
| arithmetic mean (standard deviation) | -20.5 (± 36.95) | -52.8 (± 5.74) | -31.3 (± 33.69) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 25 in Cardiopulmonary Exercise Testing (CPET) - Duration of Exercise - Modified ITT Population

| | |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------|
| End point title | Change from Baseline to Week 25 in Cardiopulmonary Exercise Testing (CPET) - Duration of Exercise - Modified ITT Population |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------|

End point description:

Subjects performed maximal incremental exercise testing using an electronically braked upright cycle ergometer. Cycle ergometry is a method of CPET that may be feasible in subjects who have orthopedic, peripheral vascular, or neurological limitations that restrict weight bearing.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 25

| End point values | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week | Modified Intent-to-Treat | |
|--------------------------------------|-----------------------|-----------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 10 | 5 | 15 | |
| Units: minutes | | | | |
| arithmetic mean (standard deviation) | 0.8 (± 0.88) | 1.1 (± 1.43) | 0.9 (± 1.05) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 52 in Cardiopulmonary Exercise Testing

(CPET) - Duration of Exercise - Modified ITT Population

| | |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------|
| End point title | Change from Baseline to Week 52 in Cardiopulmonary Exercise Testing (CPET) - Duration of Exercise - Modified ITT Population |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------|

End point description:

Subjects performed maximal incremental exercise testing using an electronically braked upright cycle ergometer. Cycle ergometry is a method of CPET that may be feasible in subjects who have orthopedic, peripheral vascular, or neurological limitations that restrict weight bearing.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 52

| End point values | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week | Modified Intent-to-Treat | |
|--------------------------------------|-----------------------|-----------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 10 | 5 | 15 | |
| Units: minutes | | | | |
| arithmetic mean (standard deviation) | 0.6 (\pm 1.34) | 0.7 (\pm 1.46) | 0.6 (\pm 1.33) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline to Week 25 in Cardiopulmonary Exercise Testing (CPET) - Peak Workload - Modified ITT Population

| | |
|-----------------|------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percent Change from Baseline to Week 25 in Cardiopulmonary Exercise Testing (CPET) - Peak Workload - Modified ITT Population |
|-----------------|------------------------------------------------------------------------------------------------------------------------------|

End point description:

Subjects performed maximal incremental exercise testing using an electronically braked upright cycle ergometer. Cycle ergometry is a method of CPET that may be feasible in subjects who have orthopedic, peripheral vascular, or neurological limitations that restrict weight bearing.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 25

| End point values | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week | Modified Intent-to-Treat | |
|--------------------------------------|-----------------------|-----------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 10 | 5 | 15 | |
| Units: % change | | | | |
| arithmetic mean (standard deviation) | 23.6 (\pm 20.87) | 38.4 (\pm 44.66) | 28.5 (\pm 30.04) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline to Week 52 in Cardiopulmonary Exercise Testing (CPET) - Peak Workload - Modified ITT Population

| | |
|-----------------|------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percent Change from Baseline to Week 52 in Cardiopulmonary Exercise Testing (CPET) - Peak Workload - Modified ITT Population |
|-----------------|------------------------------------------------------------------------------------------------------------------------------|

End point description:

Subjects performed maximal incremental exercise testing using an electronically braked upright cycle ergometer. Cycle ergometry is a method of CPET that may be feasible in subjects who have orthopedic, peripheral vascular, or neurological limitations that restrict weight bearing.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 52

| End point values | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week | Modified Intent-to-Treat | |
|--------------------------------------|-----------------------|-----------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 10 | 5 | 15 | |
| Units: % change | | | | |
| arithmetic mean (standard deviation) | 24.7 (± 26.17) | 13 (± 22.69) | 20.8 (± 24.9) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline to Week 25 in Cardiopulmonary Exercise Testing (CPET) - O2 Pulse - Modified ITT Population

| | |
|-----------------|-------------------------------------------------------------------------------------------------------------------------|
| End point title | Percent Change from Baseline to Week 25 in Cardiopulmonary Exercise Testing (CPET) - O2 Pulse - Modified ITT Population |
|-----------------|-------------------------------------------------------------------------------------------------------------------------|

End point description:

Subjects performed maximal incremental exercise testing using an electronically braked upright cycle ergometer. Cycle ergometry is a method of CPET that may be feasible in subjects who have orthopedic, peripheral vascular, or neurological limitations that restrict weight bearing.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 25

| End point values | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week | Modified Intent-to-Treat | |
|--------------------------------------|-----------------------|-----------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 10 | 5 | 15 | |
| Units: % change | | | | |
| arithmetic mean (standard deviation) | 6.8 (± 14.17) | 13.5 (± 17.65) | 9 (± 15.13) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline to Week 52 in Cardiopulmonary Exercise Testing (CPET) - O2 Pulse - Modified ITT Population

| | |
|-----------------|-------------------------------------------------------------------------------------------------------------------------|
| End point title | Percent Change from Baseline to Week 52 in Cardiopulmonary Exercise Testing (CPET) - O2 Pulse - Modified ITT Population |
|-----------------|-------------------------------------------------------------------------------------------------------------------------|

End point description:

Subjects performed maximal incremental exercise testing using an electronically braked upright cycle ergometer. Cycle ergometry is a method of CPET that may be feasible in subjects who have orthopedic, peripheral vascular, or neurological limitations that restrict weight bearing.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 52

| End point values | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week | Modified Intent-to-Treat | |
|--------------------------------------|-----------------------|-----------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 9 | 5 | 14 | |
| Units: % change | | | | |
| arithmetic mean (standard deviation) | 7.6 (± 27.89) | 2 (± 31.74) | 5.6 (± 28.22) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline to Week 25 in Cardiopulmonary Exercise Testing (CPET) - Aerobic Efficiency - Modified ITT Population

| | |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percent Change from Baseline to Week 25 in Cardiopulmonary Exercise Testing (CPET) - Aerobic Efficiency - Modified ITT Population |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------|

End point description:

Subjects performed maximal incremental exercise testing using an electronically braked upright cycle ergometer. Cycle ergometry is a method of CPET that may be feasible in subjects who have orthopedic, peripheral vascular, or neurological limitations that restrict weight bearing.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 25

| End point values | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week | Modified Intent-to-Treat | |
|--------------------------------------|-----------------------|-----------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 9 | 5 | 14 | |
| Units: % change | | | | |
| arithmetic mean (standard deviation) | -8.9 (± 15.41) | -6 (± 8.29) | -7.9 (± 13.02) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline to Week 52 in Cardiopulmonary Exercise Testing (CPET) - Aerobic Efficiency - Modified ITT Population

| | |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percent Change from Baseline to Week 52 in Cardiopulmonary Exercise Testing (CPET) - Aerobic Efficiency - Modified ITT Population |
|-----------------|-----------------------------------------------------------------------------------------------------------------------------------|

End point description:

Subjects performed maximal incremental exercise testing using an electronically braked upright cycle ergometer. Cycle ergometry is a method of CPET that may be feasible in subjects who have orthopedic, peripheral vascular, or neurological limitations that restrict weight bearing.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 52

| End point values | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week | Modified Intent-to-Treat | |
|--------------------------------------|-----------------------|-----------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 9 | 4 | 13 | |
| Units: % change | | | | |
| arithmetic mean (standard deviation) | -7.5 (± 28.39) | -9.8 (± 33.14) | -8.2 (± 28.52) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 25 in Peak Force in Muscle Strength Testing - Knee Extension Test - Modified ITT Population

| | |
|-----------------|--------------------------------------------------------------------------------------------------------------------------|
| End point title | Change from Baseline to Week 25 in Peak Force in Muscle Strength Testing - Knee Extension Test - Modified ITT Population |
|-----------------|--------------------------------------------------------------------------------------------------------------------------|

End point description:

Peak Force in the muscle strength testing using the knee extension test

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 25

| End point values | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week | Modified Intent-to-Treat | |
|--------------------------------------|-----------------------|-----------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 15 | 10 | 25 | |
| Units: newton metres | | | | |
| arithmetic mean (standard deviation) | -0.6 (± 9.76) | 5.2 (± 7.63) | 1.7 (± 9.26) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 52 in Peak Force in Muscle Strength Testing - Knee Extension Test - Modified ITT Population

| | |
|------------------------|--------------------------------------------------------------------------------------------------------------------------|
| End point title | Change from Baseline to Week 52 in Peak Force in Muscle Strength Testing - Knee Extension Test - Modified ITT Population |
| End point description: | Peak Force in the muscle strength testing using the knee extension test |
| End point type | Secondary |
| End point timeframe: | Baseline to Week 52 |

| End point values | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week | Modified Intent-to-Treat | |
|--------------------------------------|-----------------------|-----------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 13 | 9 | 22 | |
| Units: newton metres | | | | |
| arithmetic mean (standard deviation) | 3.3 (± 6.88) | 6.7 (± 8.87) | 4.7 (± 7.74) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline to Week 25 in Peak Force in Muscle Strength Testing - Knee Flexion Test - Modified ITT Population

| | |
|------------------------|--------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percent Change from Baseline to Week 25 in Peak Force in Muscle Strength Testing - Knee Flexion Test - Modified ITT Population |
| End point description: | Peak Force in the muscle strength testing using the knee flexion test |
| End point type | Secondary |

End point timeframe:

Baseline to Week 25

| End point values | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week | Modified Intent-to-Treat | |
|--------------------------------------|-----------------------|-----------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 14 | 10 | 24 | |
| Units: % change | | | | |
| arithmetic mean (standard deviation) | -4.2 (± 24.83) | 9.4 (± 44.87) | 1.5 (± 34.39) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline to Week 52 in Peak Force in Muscle Strength Testing - Knee Flexion Test - Modified ITT Population

| | |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percent Change from Baseline to Week 52 in Peak Force in Muscle Strength Testing - Knee Flexion Test - Modified ITT Population |
|-----------------|--------------------------------------------------------------------------------------------------------------------------------|

End point description:

Peak Force in the muscle strength testing using the knee flexion test

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 52

| End point values | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week | Modified Intent-to-Treat | |
|--------------------------------------|-----------------------|-----------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 12 | 9 | 21 | |
| Units: % change | | | | |
| arithmetic mean (standard deviation) | -10.8 (± 22.72) | 8.2 (± 41.57) | -2.7 (± 32.69) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline to Week 25 in Peak Force in Muscle Strength Testing - Elbow Flexion Test - Modified ITT Population

| | |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percent Change from Baseline to Week 25 in Peak Force in Muscle Strength Testing - Elbow Flexion Test - Modified ITT Population |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------|

End point description:

Peak Force in the muscle strength testing using the elbow flexion test

Percent Change from Baseline to Week 52 in Peak Force in Muscle Strength Testing - Elbow Flexion Test - Modified ITT Population

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 25

| End point values | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week | Modified Intent-to-Treat | |
|--------------------------------------|-----------------------|-----------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 12 | 7 | 19 | |
| Units: % change | | | | |
| arithmetic mean (standard deviation) | 12 (± 55.42) | 17.7 (± 41.82) | 14.1 (± 49.67) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percent Change from Baseline to Week 52 in Peak Force in Muscle Strength Testing - Elbow Flexion Test - Modified ITT Population

| | |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------|
| End point title | Percent Change from Baseline to Week 52 in Peak Force in Muscle Strength Testing - Elbow Flexion Test - Modified ITT Population |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------|

End point description:

Peak Force in the muscle strength testing using the elbow flexion test

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 52

| End point values | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week | Modified Intent-to-Treat | |
|--------------------------------------|-----------------------|-----------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 10 | 6 | 16 | |
| Units: % change | | | | |
| arithmetic mean (standard deviation) | 49.7 (± 86.83) | 50.7 (± 59.81) | 50.1 (± 75.6) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 12 in Pain Intensity measured using the

Adolescent Paediatric Pain Tool (APPT) - Modified ITT Population

| | |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Change from Baseline to Week 12 in Pain Intensity measured using the Adolescent Paediatric Pain Tool (APPT) - Modified ITT Population |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------|

End point description:

The APPT is a validated, multidimensional tool to evaluate pain in children, adolescents, and young adults. The complete APPT is measured in three parts - Part 1 of the APPT scale determines the subject's pain locations using a body template. Part 2 of the APPT scale determines the intensity of the pain using a 10 cm visual analog scale (VAS) with the lowest point of the scale (0) labeled No Pain and the highest point on the scale (10) labeled Worst Possible Pain. Intermediate regions of the scale were labeled with 3 intermediate descriptors (Little Pain, Medium Pain, and Large Pain). Part 3 of the APPT scale characterizes the pain by tracking the number and percentage of words selected by subjects to describe their pain from a total of 57 choices. Part 2 corresponds most closely to other typically used pain scales (based on VAS) and for this reason the results from Part 2 are presented here.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 12

| End point values | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week | Modified Intent-to-Treat | |
|--------------------------------------|-----------------------|-----------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 12 | 9 | 21 | |
| Units: scale units | | | | |
| arithmetic mean (standard deviation) | -2.3 (± 3.37) | -1.2 (± 2.23) | -1.8 (± 2.93) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 24 in Pain Intensity measured using the Adolescent Paediatric Pain Tool (APPT) - Modified ITT Population

| | |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Change from Baseline to Week 24 in Pain Intensity measured using the Adolescent Paediatric Pain Tool (APPT) - Modified ITT Population |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------|

End point description:

The APPT is a validated, multidimensional tool to evaluate pain in children, adolescents, and young adults. The complete APPT is measured in three parts - Part 1 of the APPT scale determines the subject's pain locations using a body template. Part 2 of the APPT scale determines the intensity of the pain using a 10 cm visual analog scale (VAS) with the lowest point of the scale (0) labeled No Pain and the highest point on the scale (10) labeled Worst Possible Pain. Intermediate regions of the scale were labeled with 3 intermediate descriptors (Little Pain, Medium Pain, and Large Pain). Part 3 of the APPT scale characterizes the pain by tracking the number and percentage of words selected by subjects to describe their pain from a total of 57 choices. Part 2 corresponds most closely to other typically used pain scales (based on VAS) and for this reason the results from Part 2 are presented here.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 24

| End point values | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week | Modified Intent-to-Treat | |
|--------------------------------------|-----------------------|-----------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 12 | 8 | 20 | |
| Units: scale units | | | | |
| arithmetic mean (standard deviation) | -2.2 (± 3.68) | -1.2 (± 2.87) | -1.8 (± 3.33) | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 52 in Pain Intensity measured using the Adolescent Paediatric Pain Tool (APPT) - Modified ITT Population

| | |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Change from Baseline to Week 52 in Pain Intensity measured using the Adolescent Paediatric Pain Tool (APPT) - Modified ITT Population |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------|

End point description:

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Baseline to Week 52

| End point values | BMN110 2.0 mg/kg/week | BMN110 4.0 mg/kg/week | Modified Intent-to-Treat | |
|--------------------------------------|-----------------------|-----------------------|--------------------------|--|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 11 | 9 | 20 | |
| Units: scale units | | | | |
| arithmetic mean (standard deviation) | -0.8 (± 3.41) | -0.8 (± 3.04) | -0.8 (± 3.17) | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Study Period

Adverse event reporting additional description:

None

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 16.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-----------------------|
| Reporting group title | BMN110 4.0 mg/kg/week |
|-----------------------|-----------------------|

Reporting group description: -

| | |
|-----------------------|-----------------------|
| Reporting group title | BMN110 2.0 mg/kg/week |
|-----------------------|-----------------------|

Reporting group description: -

| Serious adverse events | BMN110 4.0 mg/kg/week | BMN110 2.0 mg/kg/week | |
|---------------------------------------------------|-----------------------|-----------------------|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 10 (20.00%) | 3 / 15 (20.00%) | |
| number of deaths (all causes) | 0 | 0 | |
| number of deaths resulting from adverse events | | | |
| Surgical and medical procedures | | | |
| Medical device removal | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 15 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Inflammatory bowel disease | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Umbilical hernia | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Enuresis | | | |

| | | | |
|-------------------------------------------------|-----------------|----------------|--|
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Musculoskeletal and connective tissue disorders | | | |
| Knee deformity | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 15 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Kyphoscoliosis | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 2 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events | BMN110 4.0 mg/kg/week | BMN110 2.0 mg/kg/week | |
|-------------------------------------------------------|------------------------------|------------------------------|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 10 / 10 (100.00%) | 15 / 15 (100.00%) | |
| Vascular disorders | | | |
| Flushing | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Hot flush | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Hypotension | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 2 | |
| Pallor | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Peripheral coldness | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Surgical and medical procedures | | | |

| | | | |
|------------------------------------------------------------------------------------|----------------------|----------------------|--|
| Catheterisation venous subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 15 (6.67%) 1 | |
| Central venous catheterisation subjects affected / exposed occurrences (all) | 1 / 10 (10.00%) 1 | 1 / 15 (6.67%) 1 | |
| Medical device removal subjects affected / exposed occurrences (all) | 2 / 10 (20.00%) 2 | 0 / 15 (0.00%) 0 | |
| Tooth extraction subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 15 (6.67%) 2 | |
| General disorders and administration site conditions | | | |
| Catheter site pain subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 2 / 15 (13.33%) 2 | |
| Chest pain subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 2 / 15 (13.33%) 2 | |
| Chills subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 2 / 15 (13.33%) 2 | |
| Cyst subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 15 (6.67%) 1 | |
| Device malfunction subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 15 (6.67%) 1 | |
| Extravasation subjects affected / exposed occurrences (all) | 1 / 10 (10.00%) 1 | 0 / 15 (0.00%) 0 | |
| Face oedema subjects affected / exposed occurrences (all) | 1 / 10 (10.00%) 1 | 0 / 15 (0.00%) 0 | |
| Fatigue | | | |

| | | |
|-----------------------------|-----------------|-----------------|
| subjects affected / exposed | 2 / 10 (20.00%) | 8 / 15 (53.33%) |
| occurrences (all) | 5 | 12 |
| Influenza like illness | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 1 |
| Infusion site bruising | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 1 |
| Infusion site erythema | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 1 |
| Infusion site extravasation | | |
| subjects affected / exposed | 2 / 10 (20.00%) | 3 / 15 (20.00%) |
| occurrences (all) | 4 | 6 |
| Infusion site swelling | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 1 |
| Injection site pain | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 1 | 0 |
| Injection site pruritus | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 2 | 0 |
| Injection site reaction | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 1 |
| Irritability | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 2 / 15 (13.33%) |
| occurrences (all) | 0 | 3 |
| Local swelling | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 2 / 15 (13.33%) |
| occurrences (all) | 1 | 3 |
| Malaise | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 1 | 1 |
| Medical device pain | | |

| | | | |
|---------------------------------------------------------------------------------------------------------------|----------------------|-----------------------|--|
| subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 15 (6.67%) 1 | |
| Oedema peripheral subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 2 / 15 (13.33%) 2 | |
| Pain subjects affected / exposed occurrences (all) | 1 / 10 (10.00%) 1 | 2 / 15 (13.33%) 2 | |
| Pyrexia subjects affected / exposed occurrences (all) | 3 / 10 (30.00%) 9 | 9 / 15 (60.00%) 24 | |
| Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all) | 2 / 10 (20.00%) 2 | 0 / 15 (0.00%) 0 | |
| Respiratory, thoracic and mediastinal disorders Asthma subjects affected / exposed occurrences (all) | 1 / 10 (10.00%) 1 | 1 / 15 (6.67%) 2 | |
| Cough subjects affected / exposed occurrences (all) | 4 / 10 (40.00%) 8 | 6 / 15 (40.00%) 9 | |
| Dysphonia subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 15 (6.67%) 1 | |
| Dyspnoea subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 4 / 15 (26.67%) 4 | |
| Epistaxis subjects affected / exposed occurrences (all) | 1 / 10 (10.00%) 1 | 3 / 15 (20.00%) 5 | |
| Hypoventilation subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 15 (6.67%) 1 | |
| Oropharyngeal pain | | | |

| | | | |
|-----------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 4 / 10 (40.00%) | 7 / 15 (46.67%) | |
| occurrences (all) | 6 | 11 | |
| Nasal congestion | | | |
| subjects affected / exposed | 2 / 10 (20.00%) | 7 / 15 (46.67%) | |
| occurrences (all) | 2 | 9 | |
| Productive cough | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Respiratory distress | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Rhinorrhoea | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 1 | 2 | |
| Throat irritation | | | |
| subjects affected / exposed | 2 / 10 (20.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 2 | 1 | |
| Wheezing | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 2 / 15 (13.33%) | |
| occurrences (all) | 0 | 2 | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 2 / 15 (13.33%) | |
| occurrences (all) | 3 | 2 | |
| Depression | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 2 | |
| Insomnia | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 3 / 15 (20.00%) | |
| occurrences (all) | 0 | 3 | |
| Phobia | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Investigations | | | |
| Blood glucose decreased | | | |

| | | | |
|------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Haemoglobin increased | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Urine output decreased | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Urine leukocyte esterase positive | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 15 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| White blood cells urine positive | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 2 / 15 (13.33%) | |
| occurrences (all) | 0 | 2 | |
| Excoriation | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 1 | 1 | |
| Fall | | | |
| subjects affected / exposed | 2 / 10 (20.00%) | 2 / 15 (13.33%) | |
| occurrences (all) | 3 | 2 | |
| Hand fracture | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 2 / 15 (13.33%) | |
| occurrences (all) | 0 | 2 | |
| Head injury | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 2 / 15 (13.33%) | |
| occurrences (all) | 0 | 2 | |
| Inadequate analgesia | | | |

| | | | |
|--------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Infusion related reaction | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 15 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Injection related reaction | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 2 | |
| Joint injury | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Laceration | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Ligament sprain | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 15 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Limb crushing injury | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Limb injury | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 2 / 15 (13.33%) | |
| occurrences (all) | 0 | 2 | |
| Muscle strain | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Procedural pain | | | |
| subjects affected / exposed | 2 / 10 (20.00%) | 5 / 15 (33.33%) | |
| occurrences (all) | 2 | 8 | |
| Wound complication | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 15 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Congenital, familial and genetic disorders | | | |
| Pectus carinatum | | | |

| | | | |
|--------------------------------------------------|---------------------|---------------------|--|
| subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 15 (6.67%) 1 | |
| Cardiac disorders | | | |
| Bradycardia | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Sinus bradycardia | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 15 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Tachycardia | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 15 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Nervous system disorders | | | |
| Coordination abnormal | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Dizziness | | | |
| subjects affected / exposed | 2 / 10 (20.00%) | 6 / 15 (40.00%) | |
| occurrences (all) | 3 | 8 | |
| Dysgeusia | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Headache | | | |
| subjects affected / exposed | 7 / 10 (70.00%) | 13 / 15 (86.67%) | |
| occurrences (all) | 44 | 89 | |
| Lethargy | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Neuralgia | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Poor quality sleep | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Somnolence | | | |

| | | | |
|-------------------------------------------------------------------------------------------------------------|----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 2 / 15 (13.33%) 2 | |
| Syncope subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 15 (6.67%) 1 | |
| Blood and lymphatic system disorders Lymph node pain subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 15 (6.67%) 1 | |
| Ear and labyrinth disorders Ear discomfort subjects affected / exposed occurrences (all) | 1 / 10 (10.00%) 1 | 0 / 15 (0.00%) 0 | |
| Ear pruritus subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 15 (6.67%) 1 | |
| Ear pain subjects affected / exposed occurrences (all) | 2 / 10 (20.00%) 2 | 2 / 15 (13.33%) 3 | |
| Motion sickness subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 2 / 15 (13.33%) 3 | |
| Otorrhoea subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 15 (6.67%) 1 | |
| Tinnitus subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 15 (6.67%) 1 | |
| Eye disorders Eye pruritus subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 15 (6.67%) 1 | |
| Photophobia subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 15 (6.67%) 1 | |
| Vision blurred | | | |

| | | | |
|-----------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 3 | |
| Vitreous floaters | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Gastrointestinal disorders | | | |
| Abdominal discomfort | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 3 | |
| Abdominal pain | | | |
| subjects affected / exposed | 3 / 10 (30.00%) | 6 / 15 (40.00%) | |
| occurrences (all) | 23 | 18 | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 4 / 10 (40.00%) | 4 / 15 (26.67%) | |
| occurrences (all) | 11 | 8 | |
| Abdominal pain lower | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Anal pruritus | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Aerophagia | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Aphthous stomatitis | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 2 / 15 (13.33%) | |
| occurrences (all) | 0 | 2 | |
| Constipation | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 2 / 15 (13.33%) | |
| occurrences (all) | 0 | 2 | |
| Diarrhoea | | | |
| subjects affected / exposed | 4 / 10 (40.00%) | 6 / 15 (40.00%) | |
| occurrences (all) | 10 | 21 | |
| Dyspepsia | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 6 | 1 | |

| | | | |
|--------------------------------------------------------------------------------------|-----------------------|------------------------|--|
| Gastrooesophageal reflux disease subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 15 (6.67%) 1 | |
| Haematochezia subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 15 (6.67%) 1 | |
| Lip oedema subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 15 (6.67%) 1 | |
| Oral pain subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 15 (6.67%) 1 | |
| Nausea subjects affected / exposed occurrences (all) | 5 / 10 (50.00%) 6 | 10 / 15 (66.67%) 33 | |
| Swollen tongue subjects affected / exposed occurrences (all) | 1 / 10 (10.00%) 1 | 0 / 15 (0.00%) 0 | |
| Retching subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 15 (6.67%) 1 | |
| Vomiting subjects affected / exposed occurrences (all) | 5 / 10 (50.00%) 10 | 11 / 15 (73.33%) 34 | |
| Toothache subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 15 (6.67%) 1 | |
| Skin and subcutaneous tissue disorders | | | |
| Acne subjects affected / exposed occurrences (all) | 2 / 10 (20.00%) 4 | 1 / 15 (6.67%) 1 | |
| Decubitus ulcer subjects affected / exposed occurrences (all) | 0 / 10 (0.00%) 0 | 1 / 15 (6.67%) 1 | |
| Dermatitis allergic | | | |

| | | |
|-----------------------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 10 (10.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 1 | 1 |
| Dermatitis contact | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 1 |
| Ecchymosis | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 1 |
| Dry skin | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 2 | 1 |
| Eczema | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 2 / 15 (13.33%) |
| occurrences (all) | 0 | 2 |
| Erythema | | |
| subjects affected / exposed | 2 / 10 (20.00%) | 4 / 15 (26.67%) |
| occurrences (all) | 2 | 9 |
| Nail disorder | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 1 |
| Pruritus | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 3 / 15 (20.00%) |
| occurrences (all) | 1 | 6 |
| Rash | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 6 / 15 (40.00%) |
| occurrences (all) | 3 | 7 |
| Rash erythematous | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 1 | 0 |
| Rash generalised | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 1 |
| Rash pruritic | | |
| subjects affected / exposed | 2 / 10 (20.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 3 | 1 |
| Swelling face | | |

| | | | |
|-------------------------------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Urticaria | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 3 / 15 (20.00%) | |
| occurrences (all) | 0 | 11 | |
| Renal and urinary disorders | | | |
| Dysuria | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Enuresis | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 2 | |
| Pollakiuria | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 2 | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 5 / 10 (50.00%) | 6 / 15 (40.00%) | |
| occurrences (all) | 11 | 28 | |
| Back pain | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 6 / 15 (40.00%) | |
| occurrences (all) | 1 | 13 | |
| Flank pain | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Elbow deformity | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Joint swelling | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 2 / 15 (13.33%) | |
| occurrences (all) | 1 | 2 | |
| Knee deformity | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 1 | 1 | |
| Kyphoscoliosis | | | |

| | | | |
|-----------------------------|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Muscle spasms | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 3 / 15 (20.00%) | |
| occurrences (all) | 0 | 4 | |
| Musculoskeletal stiffness | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Myalgia | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 2 / 15 (13.33%) | |
| occurrences (all) | 0 | 5 | |
| Osteoarthritis | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 2 / 15 (13.33%) | |
| occurrences (all) | 0 | 2 | |
| Osteochondrosis | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Osteopenia | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Pain in extremity | | | |
| subjects affected / exposed | 4 / 10 (40.00%) | 8 / 15 (53.33%) | |
| occurrences (all) | 5 | 22 | |
| Infections and infestations | | | |
| Ear infection | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 2 / 15 (13.33%) | |
| occurrences (all) | 0 | 3 | |
| Enterobiasis | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 3 | |

| | | |
|-----------------------------|-----------------|-----------------|
| Fungal infection | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 1 |
| Gastroenteritis | | |
| subjects affected / exposed | 3 / 10 (30.00%) | 2 / 15 (13.33%) |
| occurrences (all) | 5 | 3 |
| Gastroenteritis viral | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 1 |
| Gastrointestinal infection | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 1 | 0 |
| Influenza | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 4 / 15 (26.67%) |
| occurrences (all) | 1 | 4 |
| Nasopharyngitis | | |
| subjects affected / exposed | 7 / 10 (70.00%) | 6 / 15 (40.00%) |
| occurrences (all) | 16 | 10 |
| Oral herpes | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 1 | 0 |
| Otitis media | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 2 / 15 (13.33%) |
| occurrences (all) | 1 | 2 |
| Pharyngitis | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 1 |
| Pharyngitis streptococcal | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 2 / 15 (13.33%) |
| occurrences (all) | 0 | 5 |
| Pneumonia | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 1 | 0 |
| Rhinitis | | |
| subjects affected / exposed | 2 / 10 (20.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 2 | 0 |

| | | | |
|------------------------------------|-----------------|-----------------|--|
| Sinusitis | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 5 / 10 (50.00%) | 5 / 15 (33.33%) | |
| occurrences (all) | 7 | 13 | |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Metabolism and nutrition disorders | | | |
| Decreased appetite | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 1 | 1 | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 1 / 10 (10.00%) | 0 / 15 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hypophosphataemia | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |
| Increased appetite | | | |
| subjects affected / exposed | 0 / 10 (0.00%) | 1 / 15 (6.67%) | |
| occurrences (all) | 0 | 1 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|----------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 31 July 2012 | <p>The primary changes for amending the protocol for study MOR-008 (Amendment 1)</p> <ol style="list-style-type: none">1. Language has been changed to permit the Investigator to be unblinded to a patient's treatment assignment without delay, upon their request, in the event of a serious or life-threatening adverse event for which therapy would be determined or significantly altered by knowledge of the treatment assignment. The Investigator does not need to obtain formal written approval of BioMarin's medical monitor prior to unblinding in these circumstances.2. The length of the Screening period has been extended from 14 to 21 days.3. A long-term extension phase has been added to the existing protocol.4. The language for the exclusion criterion concerning cervical spine compression has been modified.5. Language regarding the reporting of adverse events (AEs) and serious adverse events (SAEs), as well as language regarding the collection of additional samples following a severe infusion-associated reaction (IAR), has been clarified for consistency.6. The statement that 100% of the data will be source document verified has been removed.7. The collection and analysis of blood inflammatory markers was removed from this study.8. Additional minor changes have been made to improve clarity and consistency. |
| 02 August 2013 | <p>The primary reason for amending the protocol for study MOR-008 (Amendment 2)</p> <ol style="list-style-type: none">1. Dosing in the extension phase of the study has changed to an open-label 2.0 mg/kg weekly.2. The objectives in the extension phase of the study have been updated.3. After Week 96, the visit week schedule has been changed to a 48-week base, and the total length of the extension phase of the study has been changed to 166 weeks (for a total study duration up to 196 weeks).4. The Schedule of Events has been modified to streamline the collection of assessments.5. Plasma glycosaminoglycan (GAG) collection and analysis has been removed from the extension of the study.6. Information regarding previous clinical studies has been updated to include information from the Phase 3 studies, MOR-004 and MOR-005. Safety information has also been updated based on recent updates to the BMN 110 Investigator Brochure7. The BMN 110 excipients have been updated to include only those from the Phase 3/commercial formulation. Excipients found only in the Phase 1/2 drug formulation have been removed.8. The identity and contact information for the medical monitor have been updated.9. Information regarding Case Report Forms and Source Documents has been revised because patient records should be made available for source verification. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

