



Clinical trial results:

A Long-Term Study for Extended BMN 701 Treatment of Patients with Pompe Disease who have Participated in a BMN 701 Study

Summary

| | |
|--------------------------|-------------------|
| EudraCT number | 2011-001805-28 |
| Trial protocol | GB DE |
| Global end of trial date | 09 September 2016 |

Results information

| | |
|--------------------------------|-------------------|
| Result version number | v1 (current) |
| This version publication date | 28 September 2017 |
| First version publication date | 28 September 2017 |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | POM-002 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01435772 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | BioMarin Pharmaceutical Inc. |
| Sponsor organisation address | 105 Digital Drive, Novato, United States, 94949 |
| Public contact | BMN701 Clinical Program Management, BioMarin Europe Ltd., +44 0782455 2081, POMPE@bmrn.com |
| Scientific contact | BMN701 Clinical Program Management, BioMarin Europe Ltd., +44 0782455 2081, POMPE@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 | 28 July 2017 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 09 September 2016 |
| Global end of trial reached? | Yes |
| Global end of trial date | 09 September 2016 |
| Was the trial ended prematurely? | Yes |

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of the study are:

- To provide long-term, ongoing, treatment to patients who have participated in a BMN 701 clinical trial.
- To evaluate the long-term safety and tolerability both during and following BMN 701 administration;
- To determine the anti-BMN 701 antibody response to BMN 701
- To determine the anti-IGF-I and anti-IGF-II antibody response to BMN 701.

Protection of trial subjects:

The DMC reviewed the study data on a schedule defined in the DMC Charter, and offered advice on whether or not to proceed with, modify, or terminate study enrollment on the basis of toxicity. Meetings of the DMC were convened at the discretion of the DMC Chair or the Study Medical Officer.

Background therapy: -

Evidence for comparator: -

| | |
|---|----------------|
| Actual start date of recruitment | 10 August 2011 |
| 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 | Australia: 6 |
| Country: Number of subjects enrolled | France: 1 |
| Country: Number of subjects enrolled | Germany: 1 |
| Country: Number of subjects enrolled | United Kingdom: 6 |
| Country: Number of subjects enrolled | United States: 7 |
| Worldwide total number of subjects | 21 |
| EEA total number of subjects | 8 |

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) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 21 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Individuals eligible to participate in this study met all of the following criteria:

Have participated in a prior BMN 701 clinical development study;

Have been diagnosed with late-onset Pompe disease, based on the entry criteria of a prior BMN 701 study.

There were no screening failures

Period 1

| | |
|------------------------------|------------------------------|
| Period 1 title | 0-144 weeks (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

Arms

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

| | |
|------------------|---------|
| Arm title | 5 mg/kg |
|------------------|---------|

Arm description:

5 mg/kg

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | BMN 701 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate and solvent for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

BMN 701 at doses of 5 mg/kg, 10 mg/kg, or 20 mg/kg for IV administration over approximately 1.5 to 4 hours qow over repeatable 24-week treatment cycles.

| | |
|------------------|----------|
| Arm title | 10 mg/kg |
|------------------|----------|

Arm description:

10 mg/kg

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | BMN 701 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate and solvent for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

BMN 701 at doses of 5 mg/kg, 10 mg/kg, or 20 mg/kg for IV administration over approximately 1.5 to 4 hours qow over repeatable 24-week treatment cycles.

| | |
|------------------|----------|
| Arm title | 20 mg/kg |
|------------------|----------|

Arm description:

20 mg/kg

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|--|---|
| Investigational medicinal product name | BMN 701 |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Concentrate and solvent for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

BMN 701 at doses of 5 mg/kg, 10 mg/kg, or 20 mg/kg for IV administration over approximately 1.5 to 4 hours qow over repeatable 24-week treatment cycles.

| Number of subjects in period 1 | 5 mg/kg | 10 mg/kg | 20 mg/kg |
|---------------------------------------|---------|----------|----------|
| Started | 3 | 3 | 15 |
| Completed | 2 | 2 | 10 |
| Not completed | 1 | 1 | 5 |
| Consent withdrawn by subject | - | 1 | 3 |
| Adverse event | 1 | - | 2 |

Baseline characteristics

Reporting groups

| | |
|--|----------|
| Reporting group title | 5 mg/kg |
| Reporting group description: 5 mg/kg | |
| Reporting group title | 10 mg/kg |
| Reporting group description: 10 mg/kg | |
| Reporting group title | 20 mg/kg |
| Reporting group description: 20 mg/kg | |

| Reporting group values | 5 mg/kg | 10 mg/kg | 20 mg/kg |
|---|----------------|-----------------|----------------|
| Number of subjects | 3 | 3 | 15 |
| Age categorical Units: Subjects | | | |
| 18-65 | 3 | 3 | 15 |
| Age continuous Units: Years arithmetic mean standard deviation | 52.3 ± 6.66 | 42.7 ± 13.05 | 50.1 ± 5.28 |
| Gender categorical Units: Subjects | | | |
| Female | 0 | 2 | 6 |
| Male | 3 | 1 | 9 |

| Reporting group values | Total | | |
|---|-------|--|--|
| Number of subjects | 21 | | |
| Age categorical Units: Subjects | | | |
| 18-65 | 21 | | |
| Age continuous Units: Years arithmetic mean standard deviation | - | | |
| Gender categorical Units: Subjects | | | |
| Female | 8 | | |
| Male | 13 | | |

End points

End points reporting groups

| | |
|-----------------------------------|---|
| Reporting group title | 5 mg/kg |
| Reporting group description: | 5 mg/kg |
| Reporting group title | 10 mg/kg |
| Reporting group description: | 10 mg/kg |
| Reporting group title | 20 mg/kg |
| Reporting group description: | 20 mg/kg |
| Subject analysis set title | Full Analysis Set |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | The Full Analysis Set (FAS) includes all 21 subjects enrolled in POM-002 who received at least 1 dose (or a partial dose) of BMN 701. |

Primary: Anti-BMN 701 Antibody Response(Positive) to BMN 701 at Day 1

| | |
|------------------------|---|
| End point title | Anti-BMN 701 Antibody Response(Positive) to BMN 701 at Day 1 ^[1] |
| End point description: | |
| End point type | Primary |
| End point timeframe: | 0-144 weeks |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The study was terminated because BioMarin decided to end the overall development program based on competing corporate priorities. The study was not terminated for efficacy or safety reasons.

| End point values | 5 mg/kg | 10 mg/kg | 20 mg/kg | Full Analysis Set |
|-----------------------------|-----------------|-----------------|-----------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 2 | 1 | 12 | 15 |
| Units: number | 2 | 1 | 11 | 14 |

Statistical analyses

No statistical analyses for this end point

Primary: Anti-BMN 701 Antibody Response(Positive) to BMN 701 at Week 144

| | |
|------------------------|--|
| End point title | Anti-BMN 701 Antibody Response(Positive) to BMN 701 at Week 144 ^[2] |
| End point description: | |
| End point type | Primary |

End point timeframe:

0-144 weeks

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The study was terminated because BioMarin decided to end the overall development program based on competing corporate priorities. The study was not terminated for efficacy or safety reasons.

| End point values | 5 mg/kg | 10 mg/kg | 20 mg/kg | Full Analysis Set |
|-----------------------------|-----------------|-----------------|-----------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 2 | 2 | 10 | 14 |
| Units: Number | 2 | 2 | 10 | 14 |

Statistical analyses

No statistical analyses for this end point

Primary: Anti-IGF-I Antibody Response(Positive) to BMN 701 at Baseline

End point title Anti-IGF-I Antibody Response(Positive) to BMN 701 at

End point description:

End point type Primary

End point timeframe:

0-144 weeks

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The study was terminated because BioMarin decided to end the overall development program based on competing corporate priorities. The study was not terminated for efficacy or safety reasons.

| End point values | 5 mg/kg | 10 mg/kg | 20 mg/kg | Full Analysis Set |
|-----------------------------|-----------------|-----------------|-----------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 3 | 3 | 15 | 21 |
| Units: Number | 0 | 2 | 0 | 2 |

Statistical analyses

No statistical analyses for this end point

Primary: Anti-IGF-I Antibody Response(Positive) to BMN 701 at Week 144

End point title Anti-IGF-I Antibody Response(Positive) to BMN 701 at Week 144^[4]

End point description:

End point type Primary

End point timeframe:

0-144 weeks

Notes:

[4] - 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: The study was terminated because BioMarin decided to end the overall development program based on competing corporate priorities. The study was not terminated for efficacy or safety reasons.

| End point values | 5 mg/kg | 10 mg/kg | 20 mg/kg | Full Analysis Set |
|-----------------------------|-----------------|-----------------|-----------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 2 | 2 | 10 | 14 |
| Units: Number | 0 | 1 | 5 | 6 |

Statistical analyses

No statistical analyses for this end point

Primary: Anti-IGF-II Antibody Response(Positive) to BMN 701 at Baseline

| | |
|-----------------|---|
| End point title | Anti-IGF-II Antibody Response(Positive) to BMN 701 at Baseline ^[5] |
|-----------------|---|

End point description:

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

0-144 weeks

Notes:

[5] - 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: The study was terminated because BioMarin decided to end the overall development program based on competing corporate priorities. The study was not terminated for efficacy or safety reasons.

| End point values | 5 mg/kg | 10 mg/kg | 20 mg/kg | Full Analysis Set |
|-----------------------------|-----------------|-----------------|-----------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 3 | 3 | 15 | 21 |
| Units: Number | 1 | 2 | 2 | 5 |

Statistical analyses

No statistical analyses for this end point

Primary: Anti-IGF-II Antibody Response(Positive) to BMN 701 at Week 144

| | |
|-----------------|---|
| End point title | Anti-IGF-II Antibody Response(Positive) to BMN 701 at Week 144 ^[6] |
|-----------------|---|

End point description:

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

0-144 weeks

Notes:

[6] - 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: The study was terminated because BioMarin decided to end the overall development program based on competing corporate priorities. The study was not terminated for efficacy or safety reasons.

| End point values | 5 mg/kg | 10 mg/kg | 20 mg/kg | Full Analysis Set |
|-----------------------------|-----------------|-----------------|-----------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 2 | 2 | 10 | 14 |
| Units: Number | 0 | 2 | 7 | 9 |

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline - Percent Predicted MIP

End point title Baseline - Percent Predicted MIP

End point description:

End point type Secondary

End point timeframe:

0-144 weeks

| End point values | 5 mg/kg | 10 mg/kg | 20 mg/kg | Full Analysis Set |
|--------------------------------------|------------------|------------------|-----------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 0 ^[7] | 3 | 15 | 18 |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | () | 39.53 (± 21.868) | 40.2 (± 25.863) | 40.09 (± 24.641) |

Notes:

[7] - NA

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 144 - Percent Predicted MIP

End point title Change from Baseline to Week 144 - Percent Predicted MIP

End point description:

End point type Secondary

End point timeframe:

0-144 weeks

| End point values | 5 mg/kg | 10 mg/kg | 20 mg/kg | Full Analysis Set |
|--------------------------------------|------------------|------------------|------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 0 ^[8] | 2 | 11 | 13 |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | () | 21.21 (± 14.537) | 18.48 (± 18.599) | 18.89 (± 17.518) |

Notes:

[8] - NA

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline - Percent Predicted MEP

| | |
|------------------------|----------------------------------|
| End point title | Baseline - Percent Predicted MEP |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 0-144 weeks | |

| End point values | 5 mg/kg | 10 mg/kg | 20 mg/kg | Full Analysis Set |
|--------------------------------------|------------------|-----------------|-----------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 0 ^[9] | 3 | 15 | 18 |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | () | 31.07 (± 6.641) | 36.7 (± 15.939) | 35.76 (± 14.801) |

Notes:

[9] - NA

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 144 - Percent Predicted MEP

| | |
|------------------------|--|
| End point title | Change from Baseline to Week 144 - Percent Predicted MEP |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 0-144 weeks | |

| End point values | 5 mg/kg | 10 mg/kg | 20 mg/kg | Full Analysis Set |
|--------------------------------------|-------------------|-----------------|-----------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 0 ^[10] | 2 | 11 | 13 |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | () | -0.28 (± 5.841) | 5.11 (± 16.395) | 4.28 (± 15.197) |

Notes:

[10] - NA

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline - 6 Minutes Walk Test

| | |
|------------------------|--------------------------------|
| End point title | Baseline - 6 Minutes Walk Test |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 0-144 weeks | |

| End point values | 5 mg/kg | 10 mg/kg | 20 mg/kg | Full Analysis Set |
|--------------------------------------|-----------------|-----------------|-------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 3 | 3 | 15 | 21 |
| Units: meter | | | | |
| arithmetic mean (standard deviation) | 334 (± 227.119) | 360 (± 51.403) | 363.8 (± 157.818) | 359 (± 151.553) |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 144 - 6 Minutes Walk Test

| | |
|------------------------|--|
| End point title | Change from Baseline to Week 144 - 6 Minutes Walk Test |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 0-144 weeks | |

| End point values | 5 mg/kg | 10 mg/kg | 20 mg/kg | Full Analysis Set |
|--------------------------------------|---------------------|-------------------------|---------------------|------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 3 | 2 | 11 | 16 |
| Units: meter | | | | |
| arithmetic mean (standard deviation) | -36 (\pm 90.508) | -120.75 (\pm 67.529) | 9.5 (\pm 77.572) | -15.31 (\pm 86.181) |

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline - Maximum Voluntary Ventilation (MVV)

| | |
|------------------------|--|
| End point title | Baseline - Maximum Voluntary Ventilation (MVV) |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 0-144 weeks | |

| End point values | 5 mg/kg | 10 mg/kg | 20 mg/kg | Full Analysis Set |
|--------------------------------------|-------------------|--------------------|----------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 0 ^[11] | 3 | 15 | 18 |
| Units: L/min | | | | |
| arithmetic mean (standard deviation) | () | 76 (\pm 41.037) | 68.08 (\pm 26.74) | 69.4 (\pm 28.217) |

Notes:

[11] - NA

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline at Week 144 - Maximum Voluntary Ventilation (MVV)

| | |
|------------------------|--|
| End point title | Change from Baseline at Week 144 - Maximum Voluntary Ventilation (MVV) |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 0-144 weeks | |

| End point values | 5 mg/kg | 10 mg/kg | 20 mg/kg | Full Analysis Set |
|--------------------------------------|-------------------|-----------------|-----------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 0 ^[12] | 2 | 11 | 13 |
| Units: L/min | | | | |
| arithmetic mean (standard deviation) | () | 13.5 (± 13.435) | 2.24 (± 11.635) | 3.97 (± 12.073) |

Notes:

[12] - NA

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline - Percent Predicted Upright FVC

| | |
|------------------------|--|
| End point title | Baseline - Percent Predicted Upright FVC |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 0-144 weeks | |

| End point values | 5 mg/kg | 10 mg/kg | 20 mg/kg | Full Analysis Set |
|--------------------------------------|------------------|------------------|------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 3 | 3 | 15 | 21 |
| Units: Percent | | | | |
| arithmetic mean (standard deviation) | 69.33 (± 19.732) | 67.33 (± 26.577) | 57.13 (± 18.677) | 60.33 (± 19.518) |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 144 - Percent Predicted Upright FVC

| | |
|------------------------|--|
| End point title | Change from Baseline to Week 144 - Percent Predicted Upright FVC |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 0-144 weeks | |

| End point values | 5 mg/kg | 10 mg/kg | 20 mg/kg | Full Analysis Set |
|--------------------------------------|----------------------|--------------------|-----------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 3 | 2 | 11 | 16 |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | -8.33 (\pm 7.095) | -0.5 (\pm 4.95) | -2 (\pm 8) | -3 (\pm 7.633) |

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline - Percent Predicted Supine FVC

| | |
|------------------------|---|
| End point title | Baseline - Percent Predicted Supine FVC |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 0-144 weeks | |

| End point values | 5 mg/kg | 10 mg/kg | 20 mg/kg | Full Analysis Set |
|--------------------------------------|-----------------------|-----------------------|----------------------|-----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 3 | 3 | 12 | 18 |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | 36.67 (\pm 17.954) | 47.67 (\pm 32.578) | 44.25 (\pm 21.55) | 43.56 (\pm 21.794) |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 144 - Percent Predicted Supine FVC

| | |
|------------------------|---|
| End point title | Change from Baseline to Week 144 - Percent Predicted Supine FVC |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 0-144 weeks | |

| End point values | 5 mg/kg | 10 mg/kg | 20 mg/kg | Full Analysis Set |
|--------------------------------------|----------------------|---------------------|----------------------|-----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 3 | 2 | 7 | 12 |
| Units: percent | | | | |
| arithmetic mean (standard deviation) | -4.33 (\pm 9.452) | 4.5 (\pm 26.163) | -3.43 (\pm 6.901) | -2.33 (\pm 10.714) |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline to Week 144 - Urine Tetrasaccharide

| | |
|--|--|
| End point title | Change from Baseline to Week 144 - Urine Tetrasaccharide |
| End point description: 21 patients analyzed for this endpoint transitioned from the POM-001 protocol. The baseline data use to calculate the change from baseline Urine Tetrasaccharide was derived from the POM-001 study. | |
| End point type | Secondary |
| End point timeframe: 0-144 weeks | |

| End point values | 5 mg/kg | 10 mg/kg | 20 mg/kg | Full Analysis Set |
|--------------------------------------|-------------------|---------------------|----------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 0 ^[13] | 2 | 10 | 12 |
| Units: mmol/mol | | | | |
| arithmetic mean (standard deviation) | () | -0.2 (\pm 3.394) | -1.07 (\pm 0.975) | -0.93 (\pm 1.393) |

Notes:

[13] - NA

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline - IGF-I

| | |
|-------------------------------------|------------------|
| End point title | Baseline - IGF-I |
| End point description: | |
| End point type | Secondary |
| End point timeframe: 0-144 weeks | |

| End point values | 5 mg/kg | 10 mg/kg | 20 mg/kg | Full Analysis Set |
|--------------------------------------|-------------------|-------------------|-----------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 0 ^[14] | 0 ^[15] | 11 | 11 |
| Units: nmol/L | | | | |
| arithmetic mean (standard deviation) | () | () | 20.26 (± 6.465) | 20.26 (± 6.465) |

Notes:

[14] - NA

[15] - NA

Statistical analyses

No statistical analyses for this end point

Secondary: Week 144 - IGF-I

| | |
|-----------------|------------------|
| End point title | Week 144 - IGF-I |
|-----------------|------------------|

End point description:

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

End point timeframe:

0-144 weeks

| End point values | 5 mg/kg | 10 mg/kg | 20 mg/kg | Full Analysis Set |
|--------------------------------------|-----------------|-----------------|-----------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 2 | 2 | 11 | 15 |
| Units: nmol/L | | | | |
| arithmetic mean (standard deviation) | 26.98 (± 1.379) | 18.4 (± 7.078) | 17.62 (± 5.878) | 18.97 (± 6.247) |

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline - IGF-II

| | |
|-----------------|-------------------|
| End point title | Baseline - IGF-II |
|-----------------|-------------------|

End point description:

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

End point timeframe:

0-144 weeks

| End point values | 5 mg/kg | 10 mg/kg | 20 mg/kg | Full Analysis Set |
|--------------------------------------|-------------------|-----------------|--------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 0 ^[16] | 1 | 6 | 7 |
| Units: nmol/L | | | | |
| arithmetic mean (standard deviation) | () | 702 (± 0) | 496.83 (± 113.417) | 526.14 (± 129.355) |

Notes:

[16] - 20 mg/kg dose group suggested the most efficacious activity compared to other dose groups studied.

Statistical analyses

No statistical analyses for this end point

Secondary: Week 144 - IGF-II

| | |
|------------------------|-------------------|
| End point title | Week 144 - IGF-II |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 0-144 weeks | |

| End point values | 5 mg/kg | 10 mg/kg | 20 mg/kg | Full Analysis Set |
|--------------------------------------|--------------------|-------------------|--------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 3 | 2 | 11 | 11 |
| Units: nmol/L | | | | |
| arithmetic mean (standard deviation) | 467.67 (± 117.142) | 559.5 (± 140.714) | 698.82 (± 228.948) | 639.75 (± 216.405) |

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline - IGFBP3

| | |
|------------------------|-------------------|
| End point title | Baseline - IGFBP3 |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 0-144 weeks | |

| End point values | 5 mg/kg | 10 mg/kg | 20 mg/kg | Full Analysis Set |
|--------------------------------------|-------------------|-------------------|-------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 0 ^[17] | 0 ^[18] | 11 | 11 |
| Units: nmol/L | | | | |
| arithmetic mean (standard deviation) | () | () | 150.45 (± 23.914) | 150.45 (± 23.914) |

Notes:

[17] - 20 mg/kg dose group suggested the most efficacious activity compared to other dose groups studied.

[18] - 20 mg/kg dose group suggested the most efficacious activity compared to other dose groups studied.

Statistical analyses

No statistical analyses for this end point

Secondary: Week 144 - IGFBP3

| | |
|------------------------|-------------------|
| End point title | Week 144 - IGFBP3 |
| End point description: | |
| End point type | Secondary |
| End point timeframe: | |
| 0-144 weeks | |

| End point values | 5 mg/kg | 10 mg/kg | 20 mg/kg | Full Analysis Set |
|--------------------------------------|-------------------|-----------------|-------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Subject analysis set |
| Number of subjects analysed | 3 | 2 | 11 | 16 |
| Units: nmol/L | | | | |
| arithmetic mean (standard deviation) | 157.33 (± 41.477) | 209 (± 39.598) | 146.64 (± 33.587) | 156.44 (± 39.05) |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Study Period

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 19.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|---------|
| Reporting group title | 5 mg/kg |
|-----------------------|---------|

Reporting group description: -

| | |
|-----------------------|----------|
| Reporting group title | 10 mg/kg |
|-----------------------|----------|

Reporting group description: -

| | |
|-----------------------|----------|
| Reporting group title | 20 mg/kg |
|-----------------------|----------|

Reporting group description: -

| Serious adverse events | 5 mg/kg | 10 mg/kg | 20 mg/kg |
|---|----------------|----------------|-----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 3 (66.67%) | 1 / 3 (33.33%) | 7 / 15 (46.67%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | | | |
| Injury, poisoning and procedural complications | | | |
| Fall | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tendon rupture | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 0 / 15 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cardiac disorders | | | |
| Cardiac failure acute | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Myocardial infarction | | | |

| | | | |
|--|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Nervous system disorders | | | |
| Cerebrovascular accident | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Presyncope | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Immune system disorders | | | |
| Anaphylactoid reaction | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 0 / 15 (0.00%) |
| occurrences causally related to treatment / all | 2 / 2 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastrointestinal disorders | | | |
| Gastroesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Chronic respiratory failure | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 15 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory failure | | | |

| | | | |
|---|----------------|---------------|----------------|
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 0 / 15 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Stridor | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Renal and urinary disorders | | | |
| Prerenal failure | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Metabolism and nutrition disorders | | | |
| Hypoglycaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

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

| Non-serious adverse events | 5 mg/kg | 10 mg/kg | 20 mg/kg |
|---|-----------------|-----------------|-------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 3 / 3 (100.00%) | 3 / 3 (100.00%) | 15 / 15 (100.00%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Skin papilloma | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Vascular disorders | | | |
| Flushing | | | |

| | | | |
|--|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 4 / 15 (26.67%) |
| occurrences (all) | 0 | 0 | 8 |
| Haematoma | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Hot flush | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 3 (33.33%) | 4 / 15 (26.67%) |
| occurrences (all) | 1 | 1 | 4 |
| Hypertension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 3 / 15 (20.00%) |
| occurrences (all) | 0 | 0 | 6 |
| Hypotension | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 3 / 15 (20.00%) |
| occurrences (all) | 0 | 0 | 6 |
| Pallor | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 3 |
| General disorders and administration site conditions | | | |
| Application site erythema | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 2 / 15 (13.33%) |
| occurrences (all) | 0 | 0 | 2 |
| Asthenia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 2 / 15 (13.33%) |
| occurrences (all) | 0 | 0 | 2 |
| Catheter site erythema | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Catheter site inflammation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Catheter site pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 2 / 15 (13.33%) |
| occurrences (all) | 0 | 0 | 2 |
| Chest discomfort | | | |

| | | | |
|------------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 5 / 15 (33.33%) |
| occurrences (all) | 1 | 0 | 19 |
| Chest pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Chills | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 3 / 15 (20.00%) |
| occurrences (all) | 0 | 0 | 5 |
| Discomfort | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Extravasation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Fatigue | | | |
| subjects affected / exposed | 2 / 3 (66.67%) | 0 / 3 (0.00%) | 8 / 15 (53.33%) |
| occurrences (all) | 18 | 0 | 16 |
| Feeling abnormal | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 2 / 15 (13.33%) |
| occurrences (all) | 0 | 0 | 2 |
| Feeling cold | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 2 / 15 (13.33%) |
| occurrences (all) | 0 | 1 | 10 |
| Feeling hot | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 3 / 15 (20.00%) |
| occurrences (all) | 0 | 1 | 7 |
| Feeling of body temperature change | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Gait disturbance | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Influenza like illness | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Infusion site extravasation | | | |

| | | | |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Infusion site pain | | | |
| subjects affected / exposed | 2 / 3 (66.67%) | 0 / 3 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Infusion site swelling | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Malaise | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 4 / 15 (26.67%) |
| occurrences (all) | 1 | 0 | 5 |
| Non-cardiac chest pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 2 / 15 (13.33%) |
| occurrences (all) | 0 | 1 | 2 |
| Oedema peripheral | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 3 / 15 (20.00%) |
| occurrences (all) | 0 | 0 | 8 |
| Pain | | | |
| subjects affected / exposed | 2 / 3 (66.67%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 2 | 0 | 2 |
| Peripheral swelling | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 3 (33.33%) | 3 / 15 (20.00%) |
| occurrences (all) | 1 | 1 | 3 |
| Pyrexia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 2 / 15 (13.33%) |
| occurrences (all) | 0 | 0 | 2 |
| Temperature intolerance | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Tenderness | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Vessel puncture site bruise | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Immune system disorders | | | |

| | | | |
|--|---------------------|---------------------|-----------------------|
| Seasonal allergy subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 15 (6.67%) 2 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 15 (6.67%) 1 |
| Chronic respiratory failure subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 3 (33.33%) 1 | 0 / 15 (0.00%) 0 |
| Cough subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 3 / 15 (20.00%) 8 |
| Dyspnoea subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | 0 / 3 (0.00%) 0 | 9 / 15 (60.00%) 26 |
| Epistaxis subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 15 (6.67%) 2 |
| Hypoxia subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 15 (6.67%) 2 |
| Nasal congestion subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 2 / 15 (13.33%) 2 |
| Oropharyngeal pain subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | 1 / 3 (33.33%) 2 | 5 / 15 (33.33%) 12 |
| Paranasal sinus hypersecretion subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 15 (6.67%) 1 |
| Pleuritic pain subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 2 / 15 (13.33%) 2 |
| Productive cough | | | |

| | | | |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Pulmonary congestion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Rales | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Respiratory failure | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Tachypnoea | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 40 |
| Wheezing | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 4 |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 2 |
| Confusional state | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Insomnia | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 3 (33.33%) | 2 / 15 (13.33%) |
| occurrences (all) | 2 | 1 | 2 |
| Mood swings | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Nervousness | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 3 (33.33%) | 4 / 15 (26.67%) |
| occurrences (all) | 4 | 1 | 6 |
| Restlessness | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 2 / 15 (13.33%) |
| occurrences (all) | 1 | 0 | 2 |

| | | | |
|--|---------------------|---------------------|-----------------------|
| Sleep terror subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 15 (6.67%) 1 |
| Product issues Device occlusion subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 15 (6.67%) 1 |
| Investigations Ammonia increased subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 3 (33.33%) 1 | 0 / 15 (0.00%) 0 |
| Bacterial test positive subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 15 (6.67%) 2 |
| Blood calcium decreased subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 3 (33.33%) 1 | 0 / 15 (0.00%) 0 |
| Blood glucose decreased subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 7 / 15 (46.67%) 14 |
| Blood immunoglobulin E increased subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 15 (6.67%) 1 |
| Cardiac murmur subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | 0 / 3 (0.00%) 0 | 1 / 15 (6.67%) 1 |
| Complement factor increased subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 15 (6.67%) 1 |
| Lipase increased subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 15 (6.67%) 1 |
| Pulmonary physical examination abnormal subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 3 (33.33%) 1 | 0 / 15 (0.00%) 0 |
| Troponin increased | | | |

| | | | |
|--|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Tryptase increased | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 2 / 3 (66.67%) | 1 / 3 (33.33%) | 6 / 15 (40.00%) |
| occurrences (all) | 5 | 1 | 9 |
| Epicondylitis | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Eye contusion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Fall | | | |
| subjects affected / exposed | 3 / 3 (100.00%) | 2 / 3 (66.67%) | 7 / 15 (46.67%) |
| occurrences (all) | 22 | 5 | 26 |
| Head injury | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Joint injury | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Laceration | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Muscle contusion | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Muscle strain | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Post procedural contusion | | | |

| | | | |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Post procedural haemorrhage | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Procedural pain | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 2 / 15 (13.33%) |
| occurrences (all) | 2 | 0 | 2 |
| Skin abrasion | | | |
| subjects affected / exposed | 2 / 3 (66.67%) | 1 / 3 (33.33%) | 1 / 15 (6.67%) |
| occurrences (all) | 5 | 1 | 1 |
| Skin wound | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Tendon injury | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Thermal burn | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Tooth fracture | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 3 |
| Wound | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Cardiac disorders | | | |
| Bradycardia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Cardiac failure | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Diastolic dysfunction | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |

| | | | |
|--|---------------------|---------------------|-----------------------|
| Left ventricular hypertrophy subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 3 (33.33%) 1 | 0 / 15 (0.00%) 0 |
| Sinus tachycardia subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 3 / 15 (20.00%) 4 |
| Tachycardia subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | 1 / 3 (33.33%) 1 | 5 / 15 (33.33%) 49 |
| Nervous system disorders | | | |
| Balance disorder subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 15 (6.67%) 1 |
| Burning sensation subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 3 (33.33%) 1 | 2 / 15 (13.33%) 2 |
| Dizziness subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | 1 / 3 (33.33%) 5 | 8 / 15 (53.33%) 11 |
| Headache subjects affected / exposed occurrences (all) | 2 / 3 (66.67%) 7 | 1 / 3 (33.33%) 4 | 9 / 15 (60.00%) 30 |
| Hypoaesthesia subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | 1 / 3 (33.33%) 1 | 3 / 15 (20.00%) 3 |
| Lethargy subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 15 (6.67%) 1 |
| Migraine subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 1 / 3 (33.33%) 1 | 0 / 15 (0.00%) 0 |
| Paraesthesia subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 15 (6.67%) 2 |
| Presyncope | | | |

| | | | |
|--------------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Restless legs syndrome | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Sciatica | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Sinus headache | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Tremor | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 2 / 15 (13.33%) |
| occurrences (all) | 0 | 0 | 2 |
| Tunnel vision | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Ear and labyrinth disorders | | | |
| Ear discomfort | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Tinnitus | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Vertigo positional | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Eye disorders | | | |

| | | | |
|--|---------------------|---------------------|----------------------|
| Blindness transient subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 15 (6.67%) 1 |
| Ocular hyperaemia subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | 0 / 3 (0.00%) 0 | 0 / 15 (0.00%) 0 |
| Visual impairment subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 15 (6.67%) 1 |
| Gastrointestinal disorders | | | |
| Abdominal discomfort subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | 1 / 3 (33.33%) 1 | 1 / 15 (6.67%) 3 |
| Abdominal distension subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 15 (6.67%) 1 |
| Abdominal pain subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 2 / 15 (13.33%) 3 |
| Abdominal pain lower subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 15 (6.67%) 1 |
| Abdominal pain upper subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | 1 / 3 (33.33%) 1 | 3 / 15 (20.00%) 5 |
| Abdominal tenderness subjects affected / exposed occurrences (all) | 1 / 3 (33.33%) 1 | 0 / 3 (0.00%) 0 | 0 / 15 (0.00%) 0 |
| Constipation subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 3 / 15 (20.00%) 4 |
| Dental caries subjects affected / exposed occurrences (all) | 0 / 3 (0.00%) 0 | 0 / 3 (0.00%) 0 | 1 / 15 (6.67%) 1 |
| Diarrhoea | | | |

| | | | |
|----------------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 7 / 15 (46.67%) |
| occurrences (all) | 0 | 0 | 13 |
| Dyspepsia | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Flatulence | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 3 / 15 (20.00%) |
| occurrences (all) | 0 | 0 | 3 |
| Irritable bowel syndrome | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 2 / 15 (13.33%) |
| occurrences (all) | 0 | 0 | 3 |
| Nausea | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 3 (33.33%) | 6 / 15 (40.00%) |
| occurrences (all) | 1 | 1 | 29 |
| Painful defaecation | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Rectal haemorrhage | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Salivary hypersecretion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 2 / 15 (13.33%) |
| occurrences (all) | 0 | 0 | 2 |
| Tooth loss | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Toothache | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 5 |
| Vomiting | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 3 / 15 (20.00%) |
| occurrences (all) | 0 | 0 | 4 |
| Hepatobiliary disorders | | | |

| | | | |
|--|----------------|----------------|-----------------|
| Cholelithiasis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin and subcutaneous tissue disorders | | | |
| Angioedema | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Cold sweat | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 3 / 15 (20.00%) |
| occurrences (all) | 0 | 0 | 3 |
| Decubitus ulcer | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Dermal cyst | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 4 | 0 | 0 |
| Erythema | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 3 (33.33%) | 3 / 15 (20.00%) |
| occurrences (all) | 1 | 1 | 4 |
| Hyperhidrosis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 4 / 15 (26.67%) |
| occurrences (all) | 0 | 0 | 14 |
| Night sweats | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Pruritus | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 2 / 15 (13.33%) |
| occurrences (all) | 2 | 0 | 3 |
| Rash | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 2 / 3 (66.67%) | 1 / 15 (6.67%) |
| occurrences (all) | 1 | 5 | 1 |
| Rash macular | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Rash papular | | | |

| | | | |
|---|-----------------|----------------|-----------------|
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Rash pruritic | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 3 (33.33%) | 0 / 15 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Rosacea | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Skin lesion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Skin mass | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Skin ulcer | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Urticaria | | | |
| subjects affected / exposed | 3 / 3 (100.00%) | 1 / 3 (33.33%) | 2 / 15 (13.33%) |
| occurrences (all) | 8 | 1 | 3 |
| Renal and urinary disorders | | | |
| Haematuria | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 2 / 15 (13.33%) |
| occurrences (all) | 0 | 1 | 2 |
| Renal impairment | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Endocrine disorders | | | |
| Androgen deficiency | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 2 / 3 (66.67%) | 1 / 3 (33.33%) | 7 / 15 (46.67%) |
| occurrences (all) | 8 | 1 | 18 |
| Back pain | | | |

| | | | |
|--------------------------------|-----------------|----------------|-----------------|
| subjects affected / exposed | 3 / 3 (100.00%) | 1 / 3 (33.33%) | 7 / 15 (46.67%) |
| occurrences (all) | 6 | 1 | 10 |
| Bursitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Flank pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 2 / 15 (13.33%) |
| occurrences (all) | 0 | 0 | 2 |
| Groin pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Intervertebral disc protrusion | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Joint swelling | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Muscle spasms | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 3 / 15 (20.00%) |
| occurrences (all) | 1 | 0 | 9 |
| Muscle twitching | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Muscular weakness | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 2 / 15 (13.33%) |
| occurrences (all) | 1 | 0 | 2 |
| Musculoskeletal chest pain | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 1 | 0 | 1 |
| Musculoskeletal discomfort | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Musculoskeletal pain | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 2 / 15 (13.33%) |
| occurrences (all) | 1 | 0 | 3 |
| Myalgia | | | |

| | | | |
|-----------------------------|----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 3 / 15 (20.00%) |
| occurrences (all) | 0 | 0 | 4 |
| Neck pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 3 / 15 (20.00%) |
| occurrences (all) | 0 | 0 | 4 |
| Osteopenia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Pain in extremity | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 3 (33.33%) | 8 / 15 (53.33%) |
| occurrences (all) | 1 | 1 | 14 |
| Spinal pain | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Tendonitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Infections and infestations | | | |
| Blister infected | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Ear infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Fungal infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 2 / 15 (13.33%) |
| occurrences (all) | 0 | 0 | 2 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Herpes simplex | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 3 | 0 | 0 |

| | | | |
|---|----------------|----------------|-----------------|
| Influenza | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 3 / 15 (20.00%) |
| occurrences (all) | 1 | 0 | 3 |
| Lower respiratory tract infection | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 3 (33.33%) | 4 / 15 (26.67%) |
| occurrences (all) | 1 | 1 | 9 |
| Lower respiratory tract infection viral | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 2 / 15 (13.33%) |
| occurrences (all) | 0 | 0 | 2 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 4 / 15 (26.67%) |
| occurrences (all) | 0 | 1 | 7 |
| Rhinitis | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 2 / 15 (13.33%) |
| occurrences (all) | 1 | 0 | 2 |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 0 / 3 (0.00%) | 0 / 15 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 2 / 3 (66.67%) | 7 / 15 (46.67%) |
| occurrences (all) | 3 | 6 | 11 |
| Urinary tract infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 2 | 1 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 2 | 2 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 2 |
| Metabolism and nutrition disorders | | | |
| Dehydration | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 2 |
| Glucose tolerance impaired | | | |

| | | | |
|-----------------------------|----------------|----------------|------------------|
| subjects affected / exposed | 0 / 3 (0.00%) | 1 / 3 (33.33%) | 0 / 15 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Hyperglycaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 2 |
| Hyperkalaemia | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |
| Hypoglycaemia | | | |
| subjects affected / exposed | 1 / 3 (33.33%) | 1 / 3 (33.33%) | 14 / 15 (93.33%) |
| occurrences (all) | 19 | 30 | 106 |
| Iron deficiency | | | |
| subjects affected / exposed | 0 / 3 (0.00%) | 0 / 3 (0.00%) | 1 / 15 (6.67%) |
| occurrences (all) | 0 | 0 | 1 |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|--|
| 06 March 2012 | <ul style="list-style-type: none">-Pharmacokinetic assessments have been added to Week 24 (or at time of early discontinuation) for transition patients in POM-002.Additional assessments (hematology, chemistry panel, lipase, and a brief physical examination) have been added to Week -2, Day of transition, and Weeks +2 and +4 for the transition patients.-Testing of C3, C4, and CH50 at the time of an infusion-associated reaction (IAR) has been added. In addition, serum will be obtained every 6 weeks for storage for testing of C3, C4, and CH50 and other possible immunologic and inflammatory markers in the event a patient experiences an IAR.-Added option to increase BMN 701 infusion time as required.-Added option to use anti-inflammatory medications (e.g., ibuprofen) as an infusion pretreatment at the Investigator's discretion.-Added assays of insulin-like growth factor (IGF) analytes (IGF-I, IGF-II, and IGFBP3) in serum samples being collected at study visits. |
| 07 December 2012 | <ul style="list-style-type: none">-Optional desensitization regimen has been added to provide an additional treatment option for patients who experience infusion-associated reactions (IARs) that meet certain criteria.-Study size has been changed from 30-45 patients to approximately 22 patients initially, and the number of sites participating from 20 to approximately 12 initially.-The primary study objectives have been modified to include evaluation of the long-term safety and tolerability both during and following BMN 701 administration. |
| 12 August 2013 | <ul style="list-style-type: none">-An additional requirement has been added that equipment (including epinephrine) for emergency resuscitation be readily available during infusions of BMN 701.-If a patient experiences a severe IAR or an IAR requiring cessation of the BMN 701 infusion, blood is to be drawn for additional antibody assessments 4 hours (\pm 15 minutes) after the cessation of the infusion instead of "shortly" after the cessation of the infusion.-A new exploratory objective has been added to study biochemical, molecular, cellular, and genetic/genomic aspects relevant to Pompe disease from blood and urine samples obtained from patients in the study.-Laboratory testing for hemoglobin A1c levels has been added at the Week 12, Week 24, Termination, and 4-Week Post-Dose Follow-Up Visits. |
| 15 May 2015 | <ul style="list-style-type: none">-During the Transition Period visits where PK sampling is performed, an additional PK timepoint has been added at 4 hours post-infusion completion. In addition, glucose monitoring has been added at all post-completion timepoints (0.25, 0.5, 1, 2, 3, 4, 6, and 8 hours).-Clarified that urine tetrasaccharide and blood samples for evaluation of anti-drug antibodies will be done at the Week 24 assessment visit following the Transition Period to the new BMN 701 drug product.-Stopping criteria concerning hypoglycemia have been added.-The possible length of the study has been increased from 240 weeks (10 cycles) to 480 weeks (20 cycles). |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

| |
|--|
| The study was terminated because BioMarin decided to end the overall development program based on competing corporate priorities. The study was not terminated for efficacy or safety reasons. |
|--|

Notes: