# Clinical trial results:
# A Long-Term, Open-Label, Multicenter, Phase IV Study to Assess Longitudinal Changes on Height and Weight in Patients with MPS II Who Are Receiving Elaprase and Started Treatment with Elaprase at < 6 Years of Age

## Summary

| | |
|---|---|
| EudraCT number | 2014-004804-31 |
| Trial protocol | DE |
| Global end of trial date | 29 July 2025 |

**Results information**

| | |
|---|---|
| Result version number | v1 |
| This version publication date | 13 February 2026 |
| First version publication date | 13 February 2026 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | SHP-ELA-401 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT02455622 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Shire |
| Sponsor organisation address | 300 Shire Way, Lexington, MA, United States, 02421 |
| Public contact | Study Director, Takeda, TrialDisclosures@takeda.com |
| Scientific contact | Study Director, Takeda, TrialDisclosures@takeda.com |

Notes:

**Paediatric regulatory details**

| | |
|---|---|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | Yes |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 29 July 2025 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 29 July 2025 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

The main objectives of this study was to assess longitudinal changes in the following parameters in patients with MPS II who began Elaprase treatment at <6 years of age and who are receiving treatment with Elaprase:
• height
• weight

Protection of trial subjects:

Each participant or their legally authorized representative signed an informed consent form (ICF) before participating in the study

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 28 October 2015 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | Brazil: 1 |
| Country: Number of subjects enrolled | Canada: 6 |
| Country: Number of subjects enrolled | Czechia: 3 |
| Country: Number of subjects enrolled | Dominican Republic: 1 |
| Country: Number of subjects enrolled | France: 2 |
| Country: Number of subjects enrolled | Germany: 3 |
| Country: Number of subjects enrolled | Thailand: 2 |
| Country: Number of subjects enrolled | Malaysia: 2 |
| Country: Number of subjects enrolled | Netherlands: 5 |
| Country: Number of subjects enrolled | Serbia: 1 |
| Country: Number of subjects enrolled | Philippines: 2 |
| Country: Number of subjects enrolled | Poland: 1 |
| Country: Number of subjects enrolled | Spain: 2 |
| Country: Number of subjects enrolled | Viet Nam: 10 |
| Country: Number of subjects enrolled | United Kingdom: 19 |
| Country: Number of subjects enrolled | United States: 6 |
| Worldwide total number of subjects | 66 |
| EEA total number of subjects | 16 |

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) | 19 |
| Children (2-11 years) | 47 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Participants took part in the study at various investigative sites globally from 28 October 2015 to 29 July 2025.

### Pre-assignment

Screening details:

Treatment-naïve participants with mucopolysaccharidosis II(MPS II) were enrolled to receive weekly intravenous(IV) infusions of Elaprase starting at less than(<)6 years of age.Due to scarcity of treatment-naïve participants,primary growth analyses data was utilized from participants enrolled in Hunter Outcome Survey(HOS) registry for this study.

### Period 1

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

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Prospective Set |

Arm description:

Participants received once-weekly IV infusions of Elaprase at a dose of 0.5 mg/kg and were followed for a minimum of 5 years after initiation of Elaprase treatment, or until they reached their 10th birthday, whichever was longer.

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

Dosage and administration details:

Weekly Elaprase infusion from Week 1 till minimum of 5 years or until they reach their 10th birthday, whichever is longer.

| | |
|---|---|
| **Arm title** | Hunter Outcome Survey (HOS) Treated Set |

Arm description:

Treated participants from the Hunter Outcome Survey (HOS) patient registry, who met the criteria.

| | |
|---|---|
| Arm type | No intervention |

No investigational medicinal product assigned in this arm

| | |
|---|---|
| **Arm title** | HOS Untreated Set |

Arm description:

Participants in the HOS patient registry, who were not treated, were used as the comparator in the Primary Growth Analysis for this study using their height and weight data.

| | |
|---|---|
| Arm type | No intervention |

No investigational medicinal product assigned in this arm

| **Number of subjects in period 1** | Prospective Set | Hunter Outcome Survey (HOS) Treated Set | HOS Untreated Set |
|---|---|---|---|
| Started | 21 | 19 | 26 |
| Completed | 17 | 19 | 26 |
| Not completed | 4 | 0 | 0 |
| Adverse event, serious fatal | 1 | - | - |
| Reason Not Specified | 1 | - | - |
| Non-compliance with study drug | 2 | - | - |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Prospective Set |
| Reporting group description: | |
| Participants received once-weekly IV infusions of Elaprase at a dose of 0.5 mg/kg and were followed for a minimum of 5 years after initiation of Elaprase treatment, or until they reached their 10th birthday, whichever was longer. | |
| Reporting group title | Hunter Outcome Survey (HOS) Treated Set |
| Reporting group description: | |
| Treated participants from the Hunter Outcome Survey (HOS) patient registry, who met the criteria. | |
| Reporting group title | HOS Untreated Set |
| Reporting group description: | |
| Participants in the HOS patient registry, who were not treated, were used as the comparator in the Primary Growth Analysis for this study using their height and weight data. | |

| Reporting group values | Prospective Set | Hunter Outcome Survey (HOS) Treated Set | HOS Untreated Set |
|---|---|---|---|
| Number of subjects | 21 | 19 | 26 |
| Age Categorical<br>Units: Subjects | | | |
| Less than (<)2 years | 2 | 2 | 15 |
| Greater than equal to (>=) 2 years | 19 | 17 | 11 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 0 | 0 | 0 |
| Male | 21 | 19 | 26 |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | 0 |
| Asian | 15 | 1 | 1 |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | 0 |
| Black or African American | 0 | 1 | 2 |
| White | 4 | 14 | 23 |
| More than one race | 0 | 0 | 0 |
| Unknown or Not Reported | 2 | 3 | 0 |
| Ethnicity (NIH/OMB)<br>Units: Subjects | | | |
| Hispanic or Latino | 2 | 0 | 0 |
| Not Hispanic or Latino | 9 | 0 | 0 |
| Unknown or Not Reported | 10 | 19 | 26 |

| Reporting group values | Total | | |
|---|---|---|---|
| Number of subjects | 66 | | |
| Age Categorical<br>Units: Subjects | | | |
| Less than (<)2 years | 19 | | |
| Greater than equal to (>=) 2 years | 47 | | |

| | | | |
|---|---|---|---|
| Gender categorical<br>Units: Subjects | | | |
| Female | 0 | | |
| Male | 66 | | |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native | 0 | | |
| Asian | 17 | | |
| Native Hawaiian or Other Pacific Islander | 0 | | |
| Black or African American | 3 | | |
| White | 41 | | |
| More than one race | 0 | | |
| Unknown or Not Reported | 5 | | |
| Ethnicity (NIH/OMB)<br>Units: Subjects | | | |
| Hispanic or Latino | 2 | | |
| Not Hispanic or Latino | 9 | | |
| Unknown or Not Reported | 55 | | |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Prospective Set |

Reporting group description:

Participants received once-weekly IV infusions of Elaprase at a dose of 0.5 mg/kg and were followed for a minimum of 5 years after initiation of Elaprase treatment, or until they reached their 10th birthday, whichever was longer.

| | |
|---|---|
| Reporting group title | Hunter Outcome Survey (HOS) Treated Set |

Reporting group description:

Treated participants from the Hunter Outcome Survey (HOS) patient registry, who met the criteria.

| | |
|---|---|
| Reporting group title | HOS Untreated Set |

Reporting group description:

Participants in the HOS patient registry, who were not treated, were used as the comparator in the Primary Growth Analysis for this study using their height and weight data.

| | |
|---|---|
| Subject analysis set title | Combined Set |
| Subject analysis set type | Full analysis |

Subject analysis set description:

The Combined Set included data from all participants in both the Efficacy Set and the HOS Treated Set. Efficacy Set includes participants who received once-weekly IV infusions of Elaprase at a dose of 0.5 mg/kg and were followed for a minimum of 5 years after initiation of Elaprase treatment, or until they reached their 10th birthday, whichever was longer.

### Primary: Height Overall

| | |
|---|---|
| End point title | Height Overall[1] |

End point description:

The effect of treatment on growth evaluated in terms of height. The Combined Set included data from all participants in both the Efficacy Set and the HOS Treated Set. The Efficacy Set consisted of all prospective participants, who had a baseline and at least 1 post-baseline efficacy assessment. The HOS Treated Set included all participants enrolled in the HOS registry that meet the criteria. The HOS Untreated Set included untreated participants from the HOS registry that meet the criteria.

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

End point timeframe:

From Baseline through End-of-Study (approximately 9.75 years)

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

| End point values | HOS Untreated Set | Combined Set | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 26 | 40 | | |
| Units: centimeter (cm) | | | | |
| least squares mean (standard error) | 108.143 (± 1.7668) | 113.759 (± 1.211) | | |

### Statistical analyses

| | |
|---|---|
| **Statistical analysis title** | Statistical Analysis 1 |
| Comparison groups | HOS Untreated Set v Combined Set |

| | |
|---|---|
| Number of subjects included in analysis | 66 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.011 |
| Method | Linear mixed model |
| Parameter estimate | LS Mean Difference |
| Point estimate | 5.616 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | 1.329 |
| upper limit | 9.903 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 2.1497 |

## Primary: Weight Overall

| | |
|---|---|
| End point title | Weight Overall[2] |

End point description:

The effect of treatment on growth was evaluated, in terms of weight. The Combined Set included data from all participants in both the Efficacy Set and the HOS Treated Set. The Efficacy Set consisted of all prospective participants, who had a baseline and at least 1 post-baseline efficacy assessment. The HOS Treated Patients included all participants enrolled in the HOS registry that meet the criteria. The HOS Untreated Set included untreated participants from the HOS registry that meet the criteria.

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

End point timeframe:

From Baseline through End-of-Study (approximately 9.75 years)

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

| End point values | HOS Untreated Set | Combined Set | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 26 | 40 | | |
| Units: kilograms (kg) | | | | |
| least squares mean (standard error) | 26.11 (± 1.1647) | 25.164 (± 0.8382) | | |

## Statistical analyses

| | |
|---|---|
| **Statistical analysis title** | Statistical Analysis 2 |
| Comparison groups | HOS Untreated Set v Combined Set |

| | |
|---|---|
| Number of subjects included in analysis | 66 |
| Analysis specification | Pre-specified |
| Analysis type | superiority |
| P-value | = 0.5106 |
| Method | Linear mixed model |
| Parameter estimate | LS Mean Difference |
| Point estimate | -0.946 |
| Confidence interval | |
| level | 95 % |
| sides | 2-sided |
| lower limit | -3.8 |
| upper limit | 1.908 |
| Variability estimate | Standard error of the mean |
| Dispersion value | 1.4308 |

## Primary: Change from Baseline in Height Measured by Z- score

| | |
|---|---|
| End point title | Change from Baseline in Height Measured by Z- score[3][4] |

End point description:

Height Z-scores were be calculated based on the World Health Organization Drug Dictionary (WHO-DD) growth charts (for age less than or equal to (≤) 24 months) and the Centers for Disease Control and Prevention (CDC) growth charts (for age more than (>) 24 months) normal height/weight-for-age data. The Combined Set included data from all participants in both the Efficacy Set and the HOS Treated Set. The HOS Untreated Set included untreated participants from the HOS registry that meet the criteria. Subjects analyzed is the number of participants with data available for analysis for this outcome measure.

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

End point timeframe:

From Baseline through End-of-Study (approximately 9.75 years)

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: Only descriptive analyses were planned for this end point.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

| **End point values** | HOS Untreated Set | Combined Set | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 22 | 39 | | |
| Units: height z score | | | | |
| arithmetic mean (standard deviation) | -4.228 (± 1.4616) | -1.135 (± 1.3480) | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Change from Baseline in Weight Measured by Z-score

| End point title | Change from Baseline in Weight Measured by Z-score[5][6] |
|---|---|

End point description:

Weight Z-scores were calculated based on the WHO-DD growth charts (for age ≤ 24 months) and the CDC growth charts (for age >24 months) normal height/weight-for-age data. The Combined Set included data from all participants in both the Efficacy Set and the HOS Treated Set. The HOS Untreated Set included untreated participants from the HOS registry that meet the criteria. Subjects analyzed is the number of participants with data available for analysis for this outcome measure.

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

End point timeframe:

From Baseline through End-of-Study (approximately 9.75 years)

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: Only descriptive analyses were planned for this end point.

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

| **End point values** | HOS Untreated Set | Combined Set | | |
|---|---|---|---|---|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 26 | 39 | | |
| Units: weight z score | | | | |
| arithmetic mean (standard deviation) | -2.337 (± 1.9014) | -1.161 (± 1.3259) | | |

### Statistical analyses

No statistical analyses for this end point

## Primary: Number of Participants With Clinical Significant Abnormal Neurological Examination

| End point title | Number of Participants With Clinical Significant Abnormal Neurological Examination[7][8] |
|---|---|

End point description:

A full physical examination will be performed with a thorough review of body systems. Physical examinations will include a review of the patient’s general appearance, neurological examination, as well as evaluation of the body systems. Any abnormal change in findings will be recorded as an adverse event (AE). The Safety Analysis Set consisted of all prospective participants who received any amount of investigational product (IP).

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

End point timeframe:

From Screening to End-of-Study (approximately 9.75 years)

Notes:

[7] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analyses were planned for this end point.

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

| End point values | Prospective Set | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 21 | | | |
| Units: participants | 0 | | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Participants With Clinically Significant Abnormal Urinalysis Values

| End point title | Number of Participants With Clinically Significant Abnormal Urinalysis Values[9][10] |
|---|---|

End point description:

Reported here is the number of participants with clinically significant abnormal values in urinalysis tests. Only tests with at least 1 participant with clinically significant abnormal values are reported. Participant was clinically significant abnormal if there was at least one abnormal and clinically significant post-baseline value. The Safety Analysis Set consisted of all prospective participants who received any amount of IP.

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

End point timeframe:

From screening to End-of-Study (approximately 9.75 years)

Notes:

[9] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analyses were planned for this end point.

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

| End point values | Prospective Set | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 21 | | | |
| Units: participants | | | | |
| Bacteria (/High-power field (HPF)) | 5 | | | |
| Erythrocytes (/HPF) | 1 | | | |
| Glucose (milligrams per deciliter (mg/dl)) | 1 | | | |
| Leukocyte Esterase | 1 | | | |
| Mucous Threads | 1 | | | |
| Nitrite | 4 | | | |
| Occult Blood | 1 | | | |
| Protein (mg/dL) | 3 | | | |
| Specimen Appearance | 6 | | | |
| Squamous Epithelial Cells (/HPF) | 2 | | | |
| Squamous Transitional Epithelial Cells (/HPF) | 1 | | | |
| Triple Phosphate Crystals (/HPF) | 2 | | | |
| Yeast Cells | 1 | | | |
| pH (pH) | 3 | | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Participants With Treatment-emergent Adverse Events (TEAE)

| End point title | Number of Participants With Treatment-emergent Adverse Events (TEAE)[11][12] |
|---|---|

End point description:

An AE is any noxious, pathologic, or unintended change in anatomical, physiologic, or metabolic function as indicated by physical signs, symptoms, or laboratory changes occurring in any phase of a clinical study, whether or not considered product-related. This includes an exacerbation of a pre-existing condition. A TEAE is defined as an AE with an onset that occurs after receiving study drug. The Safety Analysis Set consisted of all prospective participants who received any amount of IP.

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

End point timeframe:

From screening to End-of-Study (approximately 9.75 years)

Notes:

[11] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analyses were planned for this end point.

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

| **End point values** | Prospective Set | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 21 | | | |
| Units: participants | 21 | | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number Participants With Clinically Significant Abnormal Serum Chemistry Values

| End point title | Number Participants With Clinically Significant Abnormal Serum Chemistry Values[13][14] |
|---|---|

End point description:

Reported here is the number of participants with clinically significant abnormal values in serum chemistry tests. Only tests with at least 1 participant with clinically significant abnormal values are reported. Participant was clinically significant abnormal if there was at least one abnormal and clinically significant post-baseline value. The Safety Analysis Set consisted of all prospective participants who received any amount of IP.

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

End point timeframe:

From screening to End-of-Study (approximately 9.75 years)

Notes:

[13] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analyses were planned for this end point.

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

| **End point values** | Prospective Set | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 21 | | | |
| Units: participants | | | | |
| Alanine Aminotransferase (units per liter (U/L)) | 1 | | | |
| Aspartate Aminotransferase (U/L) | 1 | | | |
| Gamma Glutamyl Transferase (U/L) | 1 | | | |

## Statistical analyses

No statistical analyses for this end point

## Primary: Number of Participants With Clinically Significant Abnormal Hematology Values

| End point title | Number of Participants With Clinically Significant Abnormal Hematology Values[15][16] |
|---|---|

End point description:

Reported here is the number of participants with clinically significant abnormal values in haematological tests. Only tests with at least 1 participant with clinically significant abnormal values are reported. Participant was clinically significant abnormal if there was at least one abnormal and clinically significant post-baseline value. The Safety Analysis Set consisted of all prospective participants who received any amount of IP.

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

End point timeframe:

Screening to End-of-Study (approximately 9.75 years)

Notes:

[15] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive analyses were planned for this end point.

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

| End point values | Prospective Set | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 21 | | | |
| Units: participants | | | | |
| Ery. Mean Corpuscular Hemoglobin (picogram (pg)) | 1 | | | |
| Ery. Mean Corpuscular Volume (femtoliter (fL)) | 1 | | | |
| Hemoglobin (gram per litre (g/L)) | 1 | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Observed Value of Height Velocity From Baseline to End of Study

| End point title | Observed Value of Height Velocity From Baseline to End of Study[17] |
|---|---|

End point description:

Height velocity was calculated as the difference in height, divided by the difference in age between consecutive study visits. BL denotes Baseline, HV denotes Height Velocity and Y denotes Years for the reported categories. Efficacy Set: all prospective participants, who had a baseline and at least 1 post-baseline efficacy assessment. Combined Set included data from all participants in both Efficacy Set and HOS Treated Set. HOS Treated Set included all participants enrolled in HOS registry that meet the criteria. HOS Untreated Set included untreated participants from HOS registry that meet the criteria. Number analysed (n) is the number of participants with data available for the specified categories.

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

End point timeframe:

From Baseline till End-of- Study Treatment (Approximately 9.75 years)

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

| End point values | Prospective Set | HOS Untreated Set | Combined Set | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 21 | 26 | 40 | |
| Units: centimeters (cm)/year | | | | |
| arithmetic mean (standard deviation) | | | | |
| Overall HV:BL to <6Y of Age (n=16,22,32) | 5.401 (± 2.5815) | 6.557 (± 2.5902) | 6.556 (± 2.6803) | |
| Overall HV:6Y of Age to EOS (n=20,18,38) | 2.699 (± 1.7610) | 1.761 (± 1.2178) | 3.571 (± 1.8064) | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Observed Value of Weight Velocity From Baseline to End of Study

| End point title | Observed Value of Weight Velocity From Baseline to End of Study[18] |
|---|---|

End point description:

Weight velocity was be calculated as the difference in weight, divided by the difference in age between consecutive study visits. Efficacy Set: all prospective participants, who had a baseline and at least 1 post-baseline efficacy assessment. Combined Set included data from all participants in both Efficacy Set and HOS Treated Set. HOS Treated Set included all participants enrolled in HOS registry that meet the criteria. HOS Untreated Set included untreated participants from HOS registry that meet criteria. BL denotes baseline, Y denotes Years and V denotes Velocity for the reported categories. Number analyzed (n) is the number of participants with data available for the specified categories.

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

End point timeframe:

From Baseline till End-of- Study Treatment (Approximately 9.75 years)

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

| **End point values** | Prospective Set | HOS Untreated Set | Combined Set | |
|---|---|---|---|---|
| Subject group type | Reporting group | Reporting group | Subject analysis set | |
| Number of subjects analysed | 21 | 26 | 40 | |
| Units: kilograms (kg)/year | | | | |
| arithmetic mean (standard deviation) | | | | |
| Overall V:BL to <6Y of Age (n=16,22,32) | 1.772 (± 1.2029) | 3.670 (± 2.0005) | 2.475 (± 1.4550) | |
| Overall V: 6Y of Age to EOS (n=20,19,38) | 1.573 (± 1.3198) | 1.445 (± 0.8324) | 2.305 (± 1.7134) | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Percent Change From Baseline for Urinary glycosaminoglycans (uGAG) Levels Normalized to Urine Creatinine

| End point title | Percent Change From Baseline for Urinary glycosaminoglycans (uGAG) Levels Normalized to Urine Creatinine[19] |
|---|---|

End point description:

Urinary GAG levels were normalized to urine creatinine (normalized uGAG) and reported as mg uGAG/ millimoles (mmol) creatinine. The Efficacy Set is defined as all prospective participants who had a baseline and at least 1 post-baseline efficacy assessment.

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

End point timeframe:

Baseline to End-of-Study (Approximately 9.75 years)

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

| End point values | Prospective Set | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 21 | | | |
| Units: mg uGAG/mmol creatinine | | | | |
| arithmetic mean (standard deviation) | | | | |
| Normalized uGAG (mg/mmol) | -70.446 (± 17.8741) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Normalized uGAG Divided by Upper Llimit of Normal for Age (uGAG/ULN) Every 12 Months

| End point title | Normalized uGAG Divided by Upper Llimit of Normal for Age (uGAG/ULN) Every 12 Months[20] |
|---|---|

End point description:

Normalized uGAG was divided by the upper limit of normal for age (uGAG/ULN), where the ULN for uGAG was obtained from Mayo Clinic. The Efficacy Set is defined as all prospective participants who had a baseline and at least 1 post-baseline efficacy assessment. Number analyzed (n) is the number of participants with data available for analysis for this outcome measure at the end-of-study. 9999 denotes Standard Deviation (SD) was not estimable for a single participant.

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

End point timeframe:

Baseline to End-of-Study (Approximately 9.75 years)

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

| End point values | Prospective Set | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 21 | | | |
| Units: Normalized uGAG/ULN | | | | |
| arithmetic mean (standard deviation) | | | | |
| Normalized uGAG/ULN: Baseline(n=20) | 5.052 (± 1.0376) | | | |
| Normalized uGAG/ULN: 12 Months(n=20) | 2.315 (± 0.7655) | | | |
| Normalized uGAG/ULN: 24 Months(n=19) | 2.096 (± 0.7657) | | | |
| Normalized uGAG/ULN: 36 Months(n=17) | 2.182 (± 0.9339) | | | |
| Normalized uGAG/ULN: 48 Months(n=17) | 2.063 (± 0.6853) | | | |
| Normalized uGAG/ULN: 60 Months(n=7) | 2.197 (± 0.8870) | | | |
| Normalized uGAG/ULN: 72 Months(n=3) | 2.190 (± 1.0945) | | | |
| Normalized uGAG/ULN: 84 Months(n=1) | 0.830 (± 9999) | | | |
| Normalized uGAG/ULN: End of Study(n=21) | 2.055 (± 1.1866) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Spleen Volume

| End point title | Spleen Volume[21] |
|---|---|

End point description:

Spleen volume was assessed using abdominal ultrasonography. Efficacy Set consisted of all prospective participants, who had a baseline and at least 1 post-baseline efficacy assessment. Subjects analyzed is the number of participants with data available for analysis. Number analyzed (n) is the number of participants with data available for analysis at the specified time points.

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

End point timeframe:

Baseline up to 24 Months

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

| **End point values** | Prospective Set | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 20 | | | |
| Units: mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Spleen Volume: Baseline (n=8) | 104.593 (± 29.9658) | | | |
| Spleen Volume: 24 Months (n=14) | 98.427 (± 47.8022) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Liver Volume

| End point title | Liver Volume[22] |
|---|---|

End point description:

Liver volume was assessed using abdominal ultrasonography. Efficacy Set consisted of all prospective participants, who had a baseline and at least 1 post-baseline efficacy assessment. Subjects analyzed is the number of participants with data available for analysis. Number analyzed (n) is the number of participants with data available for analysis at the specified time points.

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

End point timeframe:

Baseline up to 24 Months

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

| **End point values** | Prospective Set | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 20 | | | |
| Units: milliliters (mL) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Liver Volume: Baseline (n=8) | 105.855 (± 16.8925) | | | |
| Liver Volume: 24 Months (n=14) | 87.811 (± 7.0147) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Joint Mobility, as Measured by Joint Range of Motion (JROM) Scores, Including Upper-Limb and Lower-Limb Joint Scores

| End point title | Joint Mobility, as Measured by Joint Range of Motion (JROM) Scores, Including Upper-Limb and Lower-Limb Joint Scores[23] |
|---|---|

End point description:

JROM scoring followed Epps et al.'s method: joint motion (in degrees) was averaged across both sides, divided by the normal value, and multiplied by 100 to yield a percent score. These scores were then averaged to produce an overall joint score. Efficacy Set consisted of all prospective participants, who had a baseline and at least 1 post-baseline efficacy assessment. Subjects analyzed is the number of participants with data available for analysis for this outcome measure at the end-of-study.

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

End point timeframe:

From Baseline to End-of-Study (approximately 9.75 years)

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

| **End point values** | Prospective Set | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 20 | | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Lower Limb | 94.50 (± 31.634) | | | |
| Upper Limb | 104.24 (± 21.471) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Distance Walked, as Measured by Six Minute Walk Test (6MWT)

| End point title | Distance Walked, as Measured by Six Minute Walk Test |
|---|---|

End point description:

The 6MWT was conducted according to the American Thoracic Society guidelines for the 6MWT in participants who were able to walk. The distance achieved in meters was recorded. Efficacy Set consisted of all prospective participants, who had a baseline and at least 1 post-baseline efficacy assessment.

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

End point timeframe:

From Baseline to End-of-Study (approximately 9.75 years)

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

| **End point values** | Prospective Set | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 21 | | | |
| Units: meters | | | | |
| arithmetic mean (standard deviation) | | | | |
| End of Study | 224.2 (± 178.42) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Quality of Life, as Measured by Hunter-Syndrome Functional Outcome in Clinical Understanding Scale (HS-FOCUS)

| End point title | Quality of Life, as Measured by Hunter-Syndrome Functional Outcome in Clinical Understanding Scale (HS-FOCUS) [25] |
|---|---|

End point description:

The participant's QoL was assessed using the HS-FOCUS (shortened version) questionnaire. The HS-FOCUS (shortened version) questionnaire has 5 function domains (walking/standing, grip/reach, schooling/work, activities, and breathing). The scale of the 5 function domains ranges from 0 to 3, with a 3-score denoting highest disability: 0: with no difficulty;1: with some difficulty; 2: with much difficulty; 3: unable to do; Missing: Does not apply. The response option "Does not apply" is treated as "missing" with no score, the same as if the item had not been completed in the questionnaire. Higher scores indicate worse functional outcomes/greater disability. Efficacy Set consisted of all prospective participants, who had a baseline and at least 1 post-baseline efficacy assessment. Number analyzed (n) is the number of participants with data available for analysis for the specified categories.

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

End point timeframe:

Baseline to End-of-Study (Approximately 9.75 years)

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

| **End point values** | Prospective Set | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 21 | | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| End of Study: Walking/Standing (n=21) | 1.19 (± 1.042) | | | |
| End of Study: Grip/Reach (n=21) | 1.83 (± 0.986) | | | |
| End of Study: School/Work (n=17) | 1.97 (± 1.166) | | | |
| End of Study: Activities (n=20) | 1.68 (± 1.238) | | | |
| End of Study: Breathing (n=21) | 1.00 (± 0.929) | | | |

### Statistical analyses

No statistical analyses for this end point

## Secondary: Impact of Illness on Ability to Function in Daily Life, as Measured by Childhood Health Assessment Questionnaire (CHAQ Parent Report)

| End point title | Impact of Illness on Ability to Function in Daily Life, as Measured by Childhood Health Assessment Questionnaire (CHAQ Parent Report)[26] |
|---|---|

End point description:

Impact on ability to function in daily life was measured by the CHAQ (Parent Report).The CHAQ includes 30 items measured on a scale of 0 to 3: 0=without any difficulty;1=with some difficulty;2=with much difficulty;3=Unable to do;Missing: Does not apply.The highest scoring item in each category determines the score for that category with higher scores indicating worse functioning/higher disability.The mean score for the 8 subscales is the Disability Index(dressing, hygiene, arising, eating, walking, reach, grip and activities).The Discomfort Index and Health Status Index are measured on separate 15 cm scales.The distance from the left end of the scale to the respondent’s mark is measured and multiplied by 0.2 to calculate the score.Discomfort and Health Status Index scores were rescaled to 0-100 scales.Higher scores indicate greater discomfort/worse health status.Efficacy Set consisted of all prospective participants, who had a baseline and at least 1 post-baseline efficacy assessment.

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

End point timeframe:

Baseline to End-of-Study (approximately 9.75 years)

Notes:

[26] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

| **End point values** | Prospective Set | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 21 | | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Disability Index | 2.143 (± 0.7334) | | | |
| Discomfort Index | 16.4 (± 25.57) | | | |

| | | | | |
|---|---|---|---|---|
| Health Status Index | 51.9 (± 33.12) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Adaptive Behavior, as Measured by the Vineland Adaptive Behavior Scales (VABS II)

| End point title | Adaptive Behavior, as Measured by the Vineland Adaptive Behavior Scales (VABS II)[27] |
|---|---|

End point description:

Adaptive behavior was measured by the parent reported VABS-II. The scores were calculated for each of the 4 domains (communication; daily living skills; socialization; motor skills), as well as the adaptive behavior composite score. Higher scores indicate better adaptive functioning. Efficacy Set consisted of all prospective participants, who had a baseline and at least 1 post-baseline efficacy assessment. Subjects analyzed is the number of participants with data available for analysis for this outcome measure at the end-of-study.

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

End point timeframe:

Baseline to End-of-Study (approximately 9.75 years)

Notes:

[27] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

| **End point values** | Prospective Set | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 16 | | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| EOS:Adaptive Behavior Composite Standard Score | 48.1 (± 19.07) | | | |
| EOS:Communication Domain Standard Score | 44.4 (± 15.19) | | | |
| EOS:Daily Living Domain Standard Score | 51.6 (± 22.53) | | | |
| EOS:Motor Skills Domain Standard Score | 28.5 (± 13.22) | | | |
| EOS: Social Domain Standard Score | 53.6 (± 19.88) | | | |

## Statistical analyses

No statistical analyses for this end point

## Secondary: Anti-Idursulfase Antibodies (ADA) in Serum

| End point title | Anti-Idursulfase Antibodies (ADA) in Serum[28] |
|---|---|

End point description:

Blood samples were collected and analyzed for determination of anti-idursulfase antibodies every 6 months in SHP-ELA-401. Analysis of anti-idursulfase antibodies including neutralizing antibodies (NAb) was conducted using validated 3-tier immunoassay methods (screening, confirmatory, and titer). Efficacy Set consisted of all prospective participants, who had a baseline and at least 1 post-baseline efficacy assessment. Subjects analyzed is the number of participants with data available for analysis for this outcome measure at the end-of-study.

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

End point timeframe:

From Baseline to End-of-Study (Approximately 9.75 years)

Notes:

[28] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Descriptive analysis for this end point was planned only for the arm groups where it is reported.

| **End point values** | Prospective Set | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 21 | | | |
| Units: participants | | | | |
| ADA Positive (ADA+) | 21 | | | |
| NAb Positive (NAb+) | 15 | | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: | |
| From baseline until the end of study (up to approximately 9.75 years) | |
| Adverse event reporting additional description: | |
| The Safety Analysis Set consisted of all prospective participants who received any amount of IP. | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 28.0 |

| Reporting groups | |
|---|---|
| Reporting group title | Prospective Set |
| Reporting group description: | |
| Participants received once-weekly IV infusions of Elaprase at a dose of 0.5 mg/kg and were followed for a minimum of 5 years after initiation of Elaprase treatment, or until they reached their 10th birthday, whichever was longer. | |

| Serious adverse events | Prospective Set | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 11 / 21 (52.38%) | | |
| number of deaths (all causes) | 1 | | |
| number of deaths resulting from adverse events | 1 | | |
| Cardiac disorders | | | |
| Bradycardia | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Seizure | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hydrocephalus | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |

| | | | |
|---|---|---|---|
| Sudden death | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Chills | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Eye disorders | | | |
| Papilloedema | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Inguinal hernia | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Obstructive airways disorder | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Eczema | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Systemic lupus erythematosus | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Sepsis | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 6 / 21 (28.57%) | | |
| occurrences causally related to treatment / all | 0 / 8 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Influenza | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Dengue fever | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| COVID-19 | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bronchitis | | | |
| subjects affected / exposed | 3 / 21 (14.29%) | | |
| occurrences causally related to treatment / all | 0 / 6 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin infection | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Metabolism and nutrition disorders | | | |

| | | | |
|---|---|---|---|
| Hypernatraemia | | | |
| subjects affected / exposed | 1 / 21 (4.76%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| **Non-serious adverse events** | Prospective Set | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 21 / 21 (100.00%) | | |
| Injury, poisoning and procedural complications | | | |
| Skin abrasion | | | |
| subjects affected / exposed | 3 / 21 (14.29%) | | |
| occurrences (all) | 4 | | |
| Procedural pain | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences (all) | 4 | | |
| Head injury | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences (all) | 2 | | |
| Ear injury | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences (all) | 2 | | |
| Thermal burn | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences (all) | 2 | | |
| Skin laceration | | | |
| subjects affected / exposed | 3 / 21 (14.29%) | | |
| occurrences (all) | 3 | | |
| Cardiac disorders | | | |
| Aortic valve incompetence | | | |
| subjects affected / exposed | 5 / 21 (23.81%) | | |
| occurrences (all) | 5 | | |
| Mitral valve incompetence | | | |
| subjects affected / exposed | 5 / 21 (23.81%) | | |
| occurrences (all) | 5 | | |

| | | | |
|---|---|---|---|
| Nervous system disorders | | | |
| Carpal tunnel syndrome | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences (all) | 2 | | |
| Seizure | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences (all) | 2 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences (all) | 2 | | |
| General disorders and administration site conditions | | | |
| Pyrexia | | | |
| subjects affected / exposed | 11 / 21 (52.38%) | | |
| occurrences (all) | 48 | | |
| Gait disturbance | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences (all) | 2 | | |
| Eye disorders | | | |
| Blepharitis | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences (all) | 2 | | |
| Gastrointestinal disorders | | | |
| Vomiting | | | |
| subjects affected / exposed | 3 / 21 (14.29%) | | |
| occurrences (all) | 3 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 13 / 21 (61.90%) | | |
| occurrences (all) | 21 | | |
| Constipation | | | |
| subjects affected / exposed | 3 / 21 (14.29%) | | |
| occurrences (all) | 3 | | |
| Anal fissure | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences (all) | 2 | | |
| Respiratory, thoracic and mediastinal disorders | | | |

| | | | | |
|---|---|---|---|---|
| Wheezing | | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | | |
| occurrences (all) | 2 | | | |
| Rhinitis allergic | | | | |
| subjects affected / exposed | 4 / 21 (19.05%) | | | |
| occurrences (all) | 4 | | | |
| Oropharyngeal pain | | | | |
| subjects affected / exposed | 4 / 21 (19.05%) | | | |
| occurrences (all) | 5 | | | |
| Cough | | | | |
| subjects affected / exposed | 6 / 21 (28.57%) | | | |
| occurrences (all) | 11 | | | |
| Rhinorrhoea | | | | |
| subjects affected / exposed | 3 / 21 (14.29%) | | | |
| occurrences (all) | 3 | | | |
| Skin and subcutaneous tissue disorders | | | | |
| Urticaria | | | | |
| subjects affected / exposed | 6 / 21 (28.57%) | | | |
| occurrences (all) | 227 | | | |
| Dermatitis | | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | | |
| occurrences (all) | 3 | | | |
| Dermatitis allergic | | | | |
| subjects affected / exposed | 4 / 21 (19.05%) | | | |
| occurrences (all) | 4 | | | |
| Dermatitis atopic | | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | | |
| occurrences (all) | 2 | | | |
| Dermatitis diaper | | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | | |
| occurrences (all) | 2 | | | |
| Eczema | | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | | |
| occurrences (all) | 3 | | | |
| Erythema | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 3 / 21 (14.29%) | | |
| occurrences (all) | 3 | | |
| Rash | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences (all) | 2 | | |
| Rash macular | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences (all) | 4 | | |
| Psychiatric disorders | | | |
| Sleep disorder | | | |
| subjects affected / exposed | 3 / 21 (14.29%) | | |
| occurrences (all) | 3 | | |
| Infections and infestations | | | |
| Carbuncle | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences (all) | 2 | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 5 / 21 (23.81%) | | |
| occurrences (all) | 8 | | |
| Ear infection | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences (all) | 3 | | |
| Furuncle | | | |
| subjects affected / exposed | 3 / 21 (14.29%) | | |
| occurrences (all) | 4 | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 4 / 21 (19.05%) | | |
| occurrences (all) | 8 | | |
| COVID-19 | | | |
| subjects affected / exposed | 7 / 21 (33.33%) | | |
| occurrences (all) | 8 | | |
| Bronchitis | | | |
| subjects affected / exposed | 11 / 21 (52.38%) | | |
| occurrences (all) | 24 | | |
| Otitis media | | | |

| | | | | |
|---|---|---|---|---|
| subjects affected / exposed | 2 / 21 (9.52%) | | | |
| occurrences (all) | 7 | | | |
| Nasopharyngitis | | | | |
| subjects affected / exposed | 14 / 21 (66.67%) | | | |
| occurrences (all) | 96 | | | |
| Influenza | | | | |
| subjects affected / exposed | 3 / 21 (14.29%) | | | |
| occurrences (all) | 3 | | | |
| Impetigo | | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | | |
| occurrences (all) | 2 | | | |
| Viral infection | | | | |
| subjects affected / exposed | 7 / 21 (33.33%) | | | |
| occurrences (all) | 11 | | | |
| Varicella | | | | |
| subjects affected / exposed | 4 / 21 (19.05%) | | | |
| occurrences (all) | 4 | | | |
| Urinary tract infection | | | | |
| subjects affected / exposed | 6 / 21 (28.57%) | | | |
| occurrences (all) | 6 | | | |
| Upper respiratory tract infection | | | | |
| subjects affected / exposed | 13 / 21 (61.90%) | | | |
| occurrences (all) | 38 | | | |
| Tonsillitis | | | | |
| subjects affected / exposed | 5 / 21 (23.81%) | | | |
| occurrences (all) | 5 | | | |
| Sinusitis | | | | |
| subjects affected / exposed | 3 / 21 (14.29%) | | | |
| occurrences (all) | 5 | | | |
| Rhinitis | | | | |
| subjects affected / exposed | 7 / 21 (33.33%) | | | |
| occurrences (all) | 16 | | | |
| Pneumonia | | | | |
| subjects affected / exposed | 4 / 21 (19.05%) | | | |
| occurrences (all) | 5 | | | |
| Pharyngotonsillitis | | | | |

| | | | |
|---|---|---|---|
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences (all) | 2 | | |
| Pharyngitis | | | |
| subjects affected / exposed | 6 / 21 (28.57%) | | |
| occurrences (all) | 8 | | |
| Parotitis | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences (all) | 2 | | |
| Otitis media acute | | | |
| subjects affected / exposed | 3 / 21 (14.29%) | | |
| occurrences (all) | 3 | | |
| Metabolism and nutrition disorders | | | |
| Vitamin D deficiency | | | |
| subjects affected / exposed | 2 / 21 (9.52%) | | |
| occurrences (all) | 2 | | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 11 November 2015 | The following changes were made as per Amendment 01:<br>1) Added section regarding benefit/risk assessment of participants treated with Elaprase in completed clinical studies.<br>2) Added a section regarding monitoring of burden/risk to participants in this study (SHP-ELA-401).<br>3) Added a Visit window of 48 hours for completion of study activities for all visits.<br>4) Added Exclusion criterion regarding hypersensitivity to active substance or excipients for Group 1: Prospective Patient Group. 5) Allowed home infusion of Elaprase by a trained healthcare provider, with Sponsor approval. |
| 05 August 2016 | The following changes were made as per Amendment 02:<br>1) Changed planned enrollment and Primary Growth Analysis.<br>2) Added CRIM status evaluation and interpretation.<br>3) Changed study objectives.<br>4) Changed study outcome measures.<br>5) Added visit to the study schedule of events. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported