



Clinical trial results:

A Prospective, Multicenter, Single-arm, Open-label, Interventional Phase IV Study to Evaluate the Safety and Efficacy of Idursulfase (r-DNA origin) (Elaprase™) in Indian Pediatric and Adult Population with Hunter Syndrome (Mucopolysaccharidosis II)

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2022-004193-39 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 18 April 2024 |

Results information

| | |
|--------------------------------|-----------------|
| Result version number | v1 (current) |
| This version publication date | 03 January 2025 |
| First version publication date | 03 January 2025 |

Trial information

Trial identification

| | |
|-----------------------|--------------|
| Sponsor protocol code | TAK-665-4001 |
|-----------------------|--------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT05058391 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Takeda Biopharmaceuticals India Pvt. Ltd. |
| Sponsor organisation address | Building No. 8, 6th Floor, Tower C, DLF Cyber City, Gurgaon, Haryana, India, 122002 |
| 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 | 18 April 2024 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 18 April 2024 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The main purpose of this study was to evaluate the safety and efficacy of elaprase in Indian pediatric and adult participants with Hunter Syndrome.

Protection of trial subjects:

Each participant or their parents/guardians/legally authorized representatives signed an informed consent form (ICF) before participating in the study.

Background therapy: -

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 21 April 2022 |
| 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 | India: 5 |
| Worldwide total number of subjects | 5 |
| EEA total number of subjects | 0 |

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) | 4 |
| Adolescents (12-17 years) | 1 |
| 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 investigative sites in India from 21 April 2022 to 18 April 2024.

Pre-assignment

Screening details:

Participants with a diagnosis of Hunters Syndrome were enrolled in this study to receive elaprase intravenous (IV) infusion.

Period 1

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

Arms

| | |
|-----------|--------------------|
| Arm title | Elaprase 0.5 mg/kg |
|-----------|--------------------|

Arm description:

Participants received a single dose of elaprase 0.5 mg/kg IV infusion every week from Week 1 (Day 1) up to EOT at Week 52.

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

Dosage and administration details:

0.5 mg/kg IV infusion every week from Week 1 (Day 1) up to EOT at Week 52.

| | |
|---------------------------------------|--------------------|
| Number of subjects in period 1 | Elaprase 0.5 mg/kg |
| Started | 5 |
| Completed | 4 |
| Not completed | 1 |
| Adverse event, non-fatal | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--------------------|
| Reporting group title | Elaprase 0.5 mg/kg |
|-----------------------|--------------------|

Reporting group description:

Participants received a single dose of elaprase 0.5 mg/kg IV infusion every week from Week 1 (Day 1) up to EOT at Week 52.

| Reporting group values | Elaprase 0.5 mg/kg | Total | |
|------------------------|--------------------|-------|--|
| Number of subjects | 5 | 5 | |
| Age Categorical | | | |
| Units: Subjects | | | |

| | | | |
|---|--------|---|--|
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 8.0 | | |
| standard deviation | ± 4.85 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 0 | 0 | |
| Male | 5 | 5 | |
| Race (NIH/OMB) | | | |
| Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | |
| Asian | 5 | 5 | |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | |
| Black or African American | 0 | 0 | |
| White | 0 | 0 | |
| More than one race | 0 | 0 | |
| Unknown or Not Reported | 0 | 0 | |
| Ethnicity (NIH/OMB) | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 0 | 0 | |
| Not Hispanic or Latino | 5 | 5 | |
| Unknown or Not Reported | 0 | 0 | |

End points

End points reporting groups

| | |
|---|--------------------|
| Reporting group title | Elaprase 0.5 mg/kg |
| Reporting group description: | |
| Participants received a single dose of elaprase 0.5 mg/kg IV infusion every week from Week 1 (Day 1) up to EOT at Week 52. | |
| Subject analysis set title | Elaprase 0.5 mg/kg |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| Participants received a single dose of elaprase 0.5 milligrams per kilogram (mg/kg) intravenous infusion every week on Day 1 up to end of treatment (EOT) (Day 358, Week 52). | |

Primary: Number of Participants With Treatment Emergent Adverse Events (TEAEs), Serious TEAEs, Discontinuation due to TEAEs and Death

| | |
|-----------------|---|
| End point title | Number of Participants With Treatment Emergent Adverse Events (TEAEs), Serious TEAEs, Discontinuation due to TEAEs and Death ^[1] |
|-----------------|---|

End point description:

An adverse event (AE) was defined as any untoward medical occurrence in a clinical investigation participant administered a drug; it does not necessarily have to have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (example, a clinically significant abnormal laboratory value), symptom, or disease temporally associated with the use of a drug whether or not it is considered related to the drug. A serious TEAE was defined as any untoward medical occurrence that at any dose results in: death; is life-threatening; requires inpatient hospitalization or results in prolongation of existing hospitalization; persistent or significant disability/incapacity; leads to a congenital anomaly/birth defect or is an important medical event. Number of participants with TEAEs, serious TEAEs, discontinuation due to TEAEs, and death are reported. The SAS included all participants who received at least one dose of study drug at any time during trial.

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

End point timeframe:

From start of the study drug administration up to Week 53

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: Only descriptive statistics were planned for this endpoint.

| End point values | Elaprase 0.5 mg/kg | | | |
|------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 5 | | | |
| Units: participants | | | | |
| TEAEs | 5 | | | |
| Serious TEAEs | 1 | | | |
| Discontinuation due to TEAEs | 1 | | | |
| Death | 0 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Adverse Drug Reactions (ADRs)

| | |
|-----------------|--|
| End point title | Number of Participants With Adverse Drug Reactions (ADRs) ^[2] |
|-----------------|--|

End point description:

An ADR was defined as a response to a drug which was noxious and unintended, and which occurred at doses normally used in humans for prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function. The SAS included all participants who received at least one dose of study drug at any time during trial.

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

End point timeframe:

From start of the study drug administration up to Week 53

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: Only descriptive statistics were planned for this endpoint.

| | | | | |
|-----------------------------|----------------------|--|--|--|
| End point values | Elaprase 0.5 mg/kg | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 5 | | | |
| Units: participants | 1 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Infusion-related Reactions (IRRs)

| | |
|-----------------|--|
| End point title | Number of Participants With Infusion-related Reactions |
|-----------------|--|

End point description:

An IRR was defined as an AE that had been assessed as at least possibly related to treatment with elaprase and occurred during an infusion or up to 24 hours post-infusion. The SAS included all participants who received at least one dose of study drug at any time during trial.

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

End point timeframe:

From start of the study drug administration up to Week 53

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 statistics were planned for this endpoint.

| | | | | |
|-----------------------------|----------------------|--|--|--|
| End point values | Elaprase 0.5 mg/kg | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 5 | | | |
| Units: participants | 1 | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Percentage Forced Vital Capacity (%FVC) at

Weeks 27 and 53

| | |
|-----------------|--|
| End point title | Change From Baseline in Percentage Forced Vital Capacity (%FVC) at Weeks 27 and 53 |
|-----------------|--|

End point description:

FVC is the amount of air that can be forcibly exhaled from your lungs after taking the deepest breath possible, as measured by spirometry. FVC is a measure of respiratory function. The Full Analysis Set (FAS) included all enrolled participants who received at least one dose of study drug and with at least one post-baseline evaluation of any of the efficacy endpoints. Subjects analysed is the number of participants with data available for analyses.

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

End point timeframe:

Baseline, Weeks 27 and 53

| | | | | |
|--------------------------------------|----------------------|--|--|--|
| End point values | Elaprase 0.5 mg/kg | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 2 | | | |
| Units: %FVC | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 27 | -2.0 (± 4.24) | | | |
| Week 53 | 1.0 (± 2.83) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in 6 Minute Walk Test (6MWT) at Weeks 27 and 53

| | |
|-----------------|--|
| End point title | Change From Baseline in 6 Minute Walk Test (6MWT) at Weeks 27 and 53 |
|-----------------|--|

End point description:

6MWT is the distance covered over a time of 6 minutes and is a measure of physical functional capacity which is determined on a walking course. The FAS included all enrolled participants who received at least one dose of study drug and with at least one post-baseline evaluation of any of the efficacy endpoints. Subjects analysed is the number of participants with data available for analyses.

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

End point timeframe:

Baseline, Weeks 27 and 53

| | | | | |
|--------------------------------------|----------------------|--|--|--|
| End point values | Elaprase 0.5 mg/kg | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 4 | | | |
| Units: meters | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 27 | 24.3 (± 24.31) | | | |

| | | | | |
|---------|------------------|--|--|--|
| Week 53 | 184.8 (± 138.96) | | | |
|---------|------------------|--|--|--|

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Cardiac Left Ventricular Mass Index (LVMI) at Weeks 27 and 53

| | |
|-----------------|---|
| End point title | Change From Baseline in Cardiac Left Ventricular Mass Index (LVMI) at Weeks 27 and 53 |
|-----------------|---|

End point description:

Cardiac LVMI was measured by 2-dimensional (2D) echocardiography. Cardiac LVMI is the left ventricular mass (LVM) in grams indexed to body surface area (BSA), in square meters (m²). Cardiac LVMI (in grams per square meter [g/m²])=LVM divided by BSA. The FAS included all enrolled participants who received at least one dose of study drug and with at least one post-baseline evaluation of any of the efficacy endpoints. Subjects analysed is the number of participants with data available for analyses.

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

End point timeframe:

Baseline, Weeks 27 and 53

| End point values | Elaprase 0.5 mg/kg | | | |
|--------------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 4 | | | |
| Units: g/m ² | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 27 | -12.0 (± 20.91) | | | |
| Week 53 | -20.9 (± 15.59) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Left Ventricular Ejection Fraction (LVEF) at Weeks 27 and 53

| | |
|-----------------|--|
| End point title | Change From Baseline in Left Ventricular Ejection Fraction (LVEF) at Weeks 27 and 53 |
|-----------------|--|

End point description:

The LVEF was measured by 2D echocardiography and considered a sufficiently sensitive measure to evaluate any changes in cardiac function. The FAS included all enrolled participants who received at least one dose of study drug and with at least one post-baseline evaluation of any of the efficacy endpoints. Subjects analysed is the number of participants with data available for analyses.

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

End point timeframe:

Baseline, Weeks 27 and 53

| End point values | Elaprase 0.5 mg/kg | | | |
|--------------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 4 | | | |
| Units: percentage of LVEF | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 27 | 4.1 (± 3.30) | | | |
| Week 53 | 6.6 (± 7.87) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Liver Volume at Weeks 27 and 53

| | |
|-----------------|---|
| End point title | Change From Baseline in Liver Volume at Weeks 27 and 53 |
|-----------------|---|

End point description:

Liver volume was determined by Ultrasonography (USG). The FAS included all enrolled participants who received at least one dose of study drug and with at least one post-baseline evaluation of any of the efficacy endpoints. Subjects analysed is the number of participants with data available for analyses.

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

End point timeframe:

Baseline, Weeks 27 and 53

| End point values | Elaprase 0.5 mg/kg | | | |
|---|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 4 | | | |
| Units: cubic centimeters (cm ³) | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 27 | 67.0 (± 245.27) | | | |
| Week 53 | 175.3 (± 255.56) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Spleen Volume at Weeks 27 and 53

| | |
|-----------------|--|
| End point title | Change From Baseline in Spleen Volume at Weeks 27 and 53 |
|-----------------|--|

End point description:

Spleen volume was determined by USG. The FAS included all enrolled participants who received at least one dose of study drug and with at least one post-baseline evaluation of any of the efficacy endpoints. Subjects analysed is the number of participants with data available for analyses.

| | |
|---------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Weeks 27 and 53 | |

| | | | | |
|--------------------------------------|----------------------|--|--|--|
| End point values | Elaprase 0.5 mg/kg | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 4 | | | |
| Units: cm ³ | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 27 | 48.3 (± 129.60) | | | |
| Week 53 | 123.7 (± 207.15) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Normalized Urine Glycosaminoglycan (uGAG) Levels at Week 14, 27, 40, and 53

| | |
|-----------------|---|
| End point title | Change From Baseline in Normalized Urine Glycosaminoglycan (uGAG) Levels at Week 14, 27, 40, and 53 |
|-----------------|---|

End point description:

Normalized uGAG was analyzed using urine testing. The uGAG levels were normalized to urine creatinine and were reported as microgram glycosaminoglycan (GAG) per milligram creatinine (µg GAG/mg creatinine). The FAS included all enrolled participants who received at least one dose of study drug and with at least one post-baseline evaluation of any of the efficacy endpoints. 'n' indicates the number of participants with data available for analysis for the specified category.

| | |
|------------------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Weeks 14, 27, 40, and 53 | |

| | | | | |
|--------------------------------------|----------------------|--|--|--|
| End point values | Elaprase 0.5 mg/kg | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 5 | | | |
| Units: µg GAG/mg creatinine | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 14 (n=5) | 33.3 (± 112.91) | | | |
| Week 27 (n=4) | -28.9 (± 31.92) | | | |

| | | | | |
|---------------|------------------|--|--|--|
| Week 40 (n=4) | 123.4 (± 222.41) | | | |
| Week 53 (n=4) | 8.6 (± 29.50) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Global Joint Range of Motion (JROM) Score at Weeks 27 and 53

| | |
|--|--|
| End point title | Change From Baseline in Global Joint Range of Motion (JROM) Score at Weeks 27 and 53 |
| End point description: Passive joint mobility: Range of motion of shoulder, elbow, wrist, hip, knee & ankle joints, as assessed by 1 expert physician using universal goniometry method. Global JROM (% of normal range of motion) is average of 11 ratios X 100. Ratios are left/right means of passive range of motion in shoulder (flexion/extension, abduction, internal/external rotation), elbow (flexion/extension), wrist (flexion/extension), index finger (flexion/extension [combined metacarpophalangeal joint, proximal interphalangeal joint, distal interphalangeal joint motion]), hip (flexion/extension, abduction, internal/external rotation), knee (flexion/extension) & ankle (dorsiflexion) divided by normal range (American Academy of Orthopedic Surgeons and American Medical Association). FAS included all enrolled participants who received at least 1 dose of study drug and with at least one post-baseline evaluation of any of the efficacy endpoints. Subjects analysed is number of participants with data available for analyses. | |
| End point type | Secondary |
| End point timeframe: Baseline, Weeks 27 and 53 | |

| | | | | |
|---|----------------------|--|--|--|
| End point values | Elaprase 0.5 mg/kg | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 2 | | | |
| Units: percentage of normal range of motion | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 27 | -8.0 (± 7.14) | | | |
| Week 53 | -14.0 (± 0.00) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Anthropometric Parameter: Height at Weeks 27 and 53

| | |
|--|---|
| End point title | Change From Baseline in Anthropometric Parameter: Height at Weeks 27 and 53 |
| End point description: Change from baseline in height (centimeters [cm]) was assessed in participants less than (<) 18 years of | |

age. The FAS included all enrolled participants who received at least one dose of study drug and with at least one post-baseline evaluation of any of the efficacy endpoints. Subjects analysed is the number of participants with data available for analyses.

| | |
|---------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Weeks 27 and 53 | |

| | | | | |
|--------------------------------------|----------------------|--|--|--|
| End point values | Elaprase 0.5 mg/kg | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 4 | | | |
| Units: cm | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 27 | 3.0 (± 2.34) | | | |
| Week 53 | 3.7 (± 3.08) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Anthropometric Parameter: Weight at Weeks 27 and 53

| | |
|-----------------|---|
| End point title | Change From Baseline in Anthropometric Parameter: Weight at Weeks 27 and 53 |
|-----------------|---|

End point description:

Change from baseline in weight (kilograms[kg]) was assessed in all participants. The FAS included all enrolled participants who received at least one dose of study drug and with at least one post-baseline evaluation of any of the efficacy endpoints. Subjects analysed is the number of participants with data available for analyses.

| | |
|---------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Weeks 27 and 53 | |

| | | | | |
|--------------------------------------|----------------------|--|--|--|
| End point values | Elaprase 0.5 mg/kg | | | |
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 4 | | | |
| Units: kg | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 27 | 0.3 (± 1.50) | | | |
| Week 53 | 1.6 (± 1.11) | | | |

Statistical analyses

Secondary: Health-related Quality of Life (HRQoL) Based on Change From Baseline in the Hunter Syndrome-Functional Outcomes for Clinical Understanding Scale (HS-FOCUS) Domain Scores

| | |
|-----------------|---|
| End point title | Health-related Quality of Life (HRQoL) Based on Change From Baseline in the Hunter Syndrome-Functional Outcomes for Clinical Understanding Scale (HS-FOCUS) Domain Scores |
|-----------------|---|

End point description:

HS-FOCUS is developed as disease-specific measure of impact of Hunter syndrome on HRQL. HS-FOCUS is designed to gather information on participant's daily life & wellbeing, satisfaction with treatment & hospitalisations & on how Hunter syndrome impacts participant's general quality of life. HS-FOCUS includes 2 validated components: parent version & participant self-reported version for those over age 12 years. HS-FOCUS (shortened version) questionnaire has 5 function domains (walking/standing, grip/reach, school/work, activities & breathing). Items are scored using response scale from 0-3, with 0=ability to complete activity-related functions 'without any difficulty' & 3=highest disability. Higher scores on each domain indicate greater disability. FAS included all enrolled participants who received at least one dose of study drug & with at least 1 post-baseline evaluation of any of efficacy endpoints. Subjects analysed is number of participants with data available.

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

End point timeframe:

Baseline, Weeks 27 and 53

| End point values | Elaprase 0.5 mg/kg | | | |
|--------------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 4 | | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Walking/ Standing: Week 27 (n=4) | -0.3 (± 0.22) | | | |
| Walking/ Standing: Week 53 (n=4) | -0.5 (± 0.41) | | | |
| Grip/Reach: Week 27 (n=4) | -0.1 (± 0.49) | | | |
| Grip/Reach: Week 53 (n=4) | -0.1 (± 0.52) | | | |
| School/ Work: Week 27 (n=3) | 0.3 (± 0.58) | | | |
| School/ Work: Week 53 (n=3) | -1.0 (± 1.73) | | | |
| Activities: Week 27 (n=4) | -0.1 (± 0.25) | | | |
| Activities: Week 53 (n=4) | -0.9 (± 1.03) | | | |
| Breathing: Week 27 (n=4) | -0.7 (± 0.80) | | | |
| Breathing: Week 53 (n=4) | -0.8 (± 1.19) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in the HRQoL Based on Childhood Health Assessment Questionnaire (CHAQ) Domain Scores

| | |
|-----------------|---|
| End point title | Change From Baseline in the HRQoL Based on Childhood Health Assessment Questionnaire (CHAQ) Domain Scores |
|-----------------|---|

End point description:

The CHAQ was initially developed for assessing juvenile idiopathic arthritis, from the perspective of the

parent or participant, and has been previously applied to other chronic disabling conditions such as Hunter syndrome. It is a 30-item instrument that measures functional capacity and independence in activities of daily life across eight domains: dressing and grooming, arising, eating, walking, reach, grip, hygiene, and activities. For each domain, there is a 4-level difficulty scale that is scored from 0 to 3, with 0 corresponding to 'without any difficulty' and 3 to 'unable to do'. Higher scores on each domain indicate greater disability. The FAS included all enrolled participants who received at least one dose of study drug and with at least one post-baseline evaluation of any of the efficacy endpoints. Subjects analysed is the number of participants with data available for analyses.

| | |
|---------------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Baseline, Weeks 27 and 53 | |

| End point values | Elaprase 0.5 mg/kg | | | |
|--------------------------------------|----------------------|--|--|--|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 4 | | | |
| Units: score on a scale | | | | |
| arithmetic mean (standard deviation) | | | | |
| Dressing/ Grooming: Week 27 | 0.0 (\pm 2.16) | | | |
| Dressing/ Grooming: Week 53 | -0.5 (\pm 2.65) | | | |
| Arising: Week 27 | -0.3 (\pm 0.50) | | | |
| Arising: Week 53 | -0.3 (\pm 0.50) | | | |
| Eating: Week 27 | -0.3 (\pm 0.50) | | | |
| Eating: Week 53 | -0.3 (\pm 0.50) | | | |
| Walking: Week 27 | -0.3 (\pm 0.50) | | | |
| Walking: Week 53 | -0.3 (\pm 0.50) | | | |
| Hygiene: Week 27 | -0.5 (\pm 0.58) | | | |
| Hygiene: Week 53 | -0.8 (\pm 0.96) | | | |
| Reach: Week 27 | -1.0 (\pm 1.41) | | | |
| Reach: Week 53 | -0.8 (\pm 0.96) | | | |
| Grip: Week 27 | -0.5 (\pm 1.00) | | | |
| Grip: Week 53 | -1.3 (\pm 1.50) | | | |
| Activities: Week 27 | 0.0 (\pm 0.00) | | | |
| Activities: Week 53 | -0.5 (\pm 1.00) | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From start of the study drug administration up to Week 53

Adverse event reporting additional description:

The SAS included all participants who received at least one dose of study drug at any time during trial.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 27.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------------|
| Reporting group title | Elaprase 0.5 mg/kg |
|-----------------------|--------------------|

Reporting group description:

Participants received a single dose of elaprase 0.5 milligrams per kilogram (mg/kg) IV infusion every week from Week 1 (Day 1) up to end of treatment (EOT) at Week 52.

| Serious adverse events | Elaprase 0.5 mg/kg | | |
|---|--------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Infections and infestations | | | |
| Lower Respiratory Tract Infection | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

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

| Non-serious adverse events | Elaprase 0.5 mg/kg | | |
|---|--------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 5 / 5 (100.00%) | | |
| Injury, poisoning and procedural complications | | | |
| Limb Injury | | | |
| subjects affected / exposed | 1 / 5 (20.00%) | | |
| occurrences (all) | 2 | | |
| General disorders and administration site conditions | | | |

| | | | |
|--|---------------------|--|--|
| Hernia Pain subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | | |
| Infusion Site Extravasation subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 3 | | |
| Pyrexia subjects affected / exposed occurrences (all) | 3 / 5 (60.00%) 7 | | |
| Swelling subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | | |
| Ear and labyrinth disorders Ear Pain subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | | |
| Gastrointestinal disorders Abdominal Pain Upper subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | | |
| Diarrhoea subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | | |
| Mouth Ulceration subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | | |
| Vomiting subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 4 / 5 (80.00%) 6 | | |
| Asthma subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | | |

| | | | |
|---|---------------------|--|--|
| Sneezing subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | | |
| Skin and subcutaneous tissue disorders Dermatitis Allergic subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | | |
| Urticaria subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 4 | | |
| Infections and infestations Conjunctivitis subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | | |
| Ear Infection subjects affected / exposed occurrences (all) | 1 / 5 (20.00%) 1 | | |
| Nasopharyngitis subjects affected / exposed occurrences (all) | 4 / 5 (80.00%) 8 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 24 February 2021 | The following changes were made as per amendment 2.0: 1. Updated study inclusion, exclusion and discontinuation criteria. |
| 27 October 2022 | The following changes were made as per amendment 3.0 1. Changed the sponsor's name from "Shire Biotech India Pvt. Ltd." to "Takeda Biopharmaceuticals India Pvt. Ltd." and updated all the relevant contact |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported