



Clinical trial results:

A Multi-Center, Open-Label Study Evaluating Safety and Clinical Outcomes in Hunter Syndrome subjects 5 Years of Age and Younger Receiving Idursulfase Enzyme Replacement Therapy

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2007-006044-22 |
| Trial protocol | PL |
| Global end of trial date | 08 July 2011 |

Results information

| | |
|--------------------------------|-------------------|
| Result version number | v1 (current) |
| This version publication date | 04 September 2018 |
| First version publication date | 24 June 2015 |

Trial information

Trial identification

| | |
|-----------------------|-------------|
| Sponsor protocol code | HGT-ELA-038 |
|-----------------------|-------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00607386 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | Shire Human Genetic Therapies, Inc. (Shire HGT) |
| Sponsor organisation address | 300 Shire Way, Lexington , MA 02421, United States, |
| Public contact | Arian Pano, Shire HGT, apano@shire.com |
| Scientific contact | Arian Pano, Shire HGT, apano@shire.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 | 08 July 2011 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|--------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 08 July 2011 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

To determine the safety of once-weekly dosing of idursulfase (Elaprase®) 0.5 milligram per kilogram (mg/kg) administered by intravenous (IV) infusion for male Hunter syndrome subjects less than or equal to (\leq) 5 years old.

Protection of trial subjects:

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with good clinical practice and applicable regulatory requirements. Known instances of nonconformance were documented and were not considered to have an impact on the overall conclusions of this study.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 31 December 2007 |
| 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: 15 |
| Country: Number of subjects enrolled | Poland: 12 |
| Country: Number of subjects enrolled | Taiwan: 3 |
| Worldwide total number of subjects | 30 |
| EEA total number of subjects | 12 |

Notes:

Subjects enrolled per age group

| | |
|---|----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 4 |
| Children (2-11 years) | 26 |
| 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: -

Pre-assignment

Screening details:

A total of 30 subjects were enrolled of which 28 subjects received study drug.

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 | Idursulfase |
|------------------|-------------|

Arm description:

Open-label treatment with idursulfase

| | |
|--|-----------------|
| Arm type | Experimental |
| Investigational medicinal product name | Idursulfase |
| Investigational medicinal product code | |
| Other name | Elaprase |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Idursulfase was administered every week at a dose of 0.5 mg/kg by continuous IV infusion over a minimum of 3 hours. The dose of drug was calculated based on the subject's weight at each visit. Subjects received their first treatment at Week 1 and every week thereafter for 1 year up to a maximum of 52 infusions for the duration of the study.

| Number of subjects in period 1 | Idursulfase |
|--------------------------------|-------------|
| Started | 28 |
| Completed | 27 |
| Not completed | 1 |
| Physician decision | 1 |

Baseline characteristics

Reporting groups^[1]

| | |
|-----------------------|-------------|
| Reporting group title | Idursulfase |
|-----------------------|-------------|

Reporting group description:

Open-label treatment with idursulfase

Notes:

[1] - The number of subjects reported to be in the baseline period is not equal to the worldwide number of subjects enrolled in the trial. It is expected that these numbers will be the same.

Justification: Not all the enrolled subjects were treated with study drug. As baseline included only treated subjects, the worldwide number enrolled in the trial differs with the number of subjects reported in the baseline period.

| Reporting group values | Idursulfase | Total | |
|--|-------------|-------|--|
| Number of subjects | 28 | 28 | |
| Age categorical | | | |
| Units: Subjects | | | |
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | 4 | | |
| standard deviation | ± 1.62 | - | |
| Gender Categorical | | | |
| Units: subjects | | | |
| Male | 28 | 28 | |
| Baseline Normalized Urinary Glycosaminoglycan (GAG) Level | | | |
| Units: micogram/milligram creatinine | | | |
| arithmetic mean | 738.3 | | |
| standard deviation | ± 165.21 | - | |

End points

End points reporting groups

| | |
|---|---------------------------------|
| Reporting group title | Idursulfase |
| Reporting group description: | |
| Open-label treatment with idursulfase | |
| Subject analysis set title | Pharmacokinetic (PK) Population |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| All enrolled subjects who had at least one serum concentration measurement available. | |
| Subject analysis set title | Safety Population |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| All enrolled subjects who received at least one study dose (or any portion of a dose) of idursulfase. | |

Primary: Safety Evaluation

| | |
|---|----------------------------------|
| End point title | Safety Evaluation ^[1] |
| End point description: | |
| An adverse event (AE) was defined as any untoward medical occurrence in a clinical investigation participant administered as a pharmaceutical product that did not necessarily have a causal relationship with this treatment. A serious adverse event (SAE) was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Number of subjects with AEs occurred after start of study treatment until 30 days after the last infusion of idursulfase, were reported. | |
| End point type | Primary |
| End point timeframe: | |
| From the start of study treatment until 30 days after the last infusion of idursulfase | |

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: Descriptive statistics were done, no inferential statistical analyses were performed.

| End point values | Idursulfase | | | |
|--|-------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 28 ^[2] | | | |
| Units: subjects | | | | |
| number (not applicable) | | | | |
| Experienced at least one adverse event (AE) | 28 | | | |
| Deaths | 0 | | | |
| Discontinued due to an AE | 0 | | | |
| Experienced at least one drug-related AE | 16 | | | |
| Experienced at least one serious AE (SAE) | 13 | | | |
| Experienced at least one severe AE | 2 | | | |
| Experienced at least one infusion-related AE | 16 | | | |

Notes:

[2] - Safety population.

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change from Baseline to Week 53 in Normalized Urinary Glycosaminoglycan (GAG) Levels

| | |
|-----------------|---|
| End point title | Mean Change from Baseline to Week 53 in Normalized Urinary Glycosaminoglycan (GAG) Levels |
|-----------------|---|

End point description:

Analysis of urinary GAG levels was performed at baseline, Week 18, Week 36, and Week 53 as an assessment of the pharmacodynamic effects of Elaprase (idursulfase). In the categories listed below, 'N' signifies the number of subjects evaluable for the timepoint.

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

End point timeframe:

Baseline, Weeks 18, 36 and 53

| End point values | Idursulfase | | | |
|--|-------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 28 ^[3] | | | |
| Units: microgram/milligram creatinine arithmetic mean (standard deviation) | | | | |
| Baseline (N=28) | 738.3 (± 165.21) | | | |
| Change at Week 18 (N=27) | -368 (± 165.44) | | | |
| Change at Week 36 (N=27) | -400.3 (± 180.27) | | | |
| Change at Week 53 (N=27) | -402.4 (± 162.13) | | | |

Notes:

[3] - Safety population.

Statistical analyses

No statistical analyses for this end point

Secondary: Single- and Repeat-Dose Pharmacokinetics - Maximum Observed Serum Concentration (C_{max})

| | |
|-----------------|---|
| End point title | Single- and Repeat-Dose Pharmacokinetics - Maximum Observed Serum Concentration (C _{max}) |
|-----------------|---|

End point description:

In the categories listed below, "N" signifies the number of subjects evaluable for the timepoint.

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

End point timeframe:

Weeks 1 and 27

| | | | | |
|--------------------------------------|-------------------|--|--|--|
| End point values | Idursulfase | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 27 ^[4] | | | |
| Units: nanogram per milliliter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 1 (N=27) | 1333 (± 817) | | | |
| Week 27 (N=19) | 1032 (± 590) | | | |

Notes:

[4] - PK population.

Statistical analyses

No statistical analyses for this end point

Secondary: Single- and Repeat-Dose Pharmacokinetics - Time of Maximum Observed Serum Concentration (Tmax)

| | |
|-----------------|--|
| End point title | Single- and Repeat-Dose Pharmacokinetics - Time of Maximum Observed Serum Concentration (Tmax) |
|-----------------|--|

End point description:

In the categories listed below, "N" signifies the number of subjects evaluable for the timepoint.

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

End point timeframe:

Weeks 1 and 27

| | | | | |
|--------------------------------------|-------------------|--|--|--|
| End point values | Idursulfase | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 27 ^[5] | | | |
| Units: minutes | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 1 (N=27) | 163 (± 28) | | | |
| Week 27 (N=19) | 167 (± 32) | | | |

Notes:

[5] - PK population.

Statistical analyses

No statistical analyses for this end point

Secondary: Single- and Repeat-Dose Pharmacokinetics - Area Under the Serum Concentration-Time Curve from Time 0 to the Final Time Point with a Concentration of at Least Lower Limit of Quantitation (AUClast)

| | |
|-----------------|---|
| End point title | Single- and Repeat-Dose Pharmacokinetics - Area Under the Serum Concentration-Time Curve from Time 0 to the Final Time Point with a Concentration of at Least Lower Limit of Quantitation (AUClast) |
|-----------------|---|

End point description:

In the categories listed below, "N" signifies the number of subjects evaluable for the timepoint.

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

End point timeframe:

Weeks 1 and 27

| | | | | |
|---------------------------------------|-------------------|--|--|--|
| End point values | Idursulfase | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 27 ^[6] | | | |
| Units: minute*nanogram per milliliter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 1 (N=27) | 196526 (± 71779) | | | |
| Week 27 (N=19) | 174869 (± 109118) | | | |

Notes:

[6] - PK population.

Statistical analyses

No statistical analyses for this end point

Secondary: Single- and Repeat-Dose Pharmacokinetics - Area Under the Serum Concentration-Time Curve from Time 0 to Infinity (AUCinf)

| | |
|-----------------|---|
| End point title | Single- and Repeat-Dose Pharmacokinetics - Area Under the Serum Concentration-Time Curve from Time 0 to Infinity (AUCinf) |
|-----------------|---|

End point description:

In the categories listed below, "N" signifies the number of subjects evaluable for the timepoint.

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

End point timeframe:

Weeks 1 and 27

| | | | | |
|---------------------------------------|-------------------|--|--|--|
| End point values | Idursulfase | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 26 ^[7] | | | |
| Units: minute*nanogram per milliliter | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 1 (N=26) | 224343 (± 76944) | | | |
| Week 27 (N=18) | 201130 (± 117575) | | | |

Notes:

[7] - PK population with evaluable subjects for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Single- and Repeat-Dose Pharmacokinetics - Elimination Half-Life (t_{1/2})

| | |
|-----------------|--|
| End point title | Single- and Repeat-Dose Pharmacokinetics - Elimination Half-Life (t _{1/2}) |
|-----------------|--|

End point description:

t_{1/2} refers to the elimination of the drug. It is the time taken for the blood plasma concentration to reach half the concentration in the terminal phase of elimination. It is expressed in hours and derived from the terminal slope of the concentration versus time curve. In the categories listed below, "N" signifies the number of subjects evaluable for the timepoint.

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

End point timeframe:

Weeks 1 and 27

| | | | | |
|--------------------------------------|-------------------|--|--|--|
| End point values | Idursulfase | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 26 ^[8] | | | |
| Units: minutes | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 1 (N=26) | 160 (± 69) | | | |
| Week 27 (N=18) | 109 (± 43) | | | |

Notes:

[8] - PK population with evaluable subjects for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Single- and Repeat-Dose Pharmacokinetics - Mean Residence Time from Time 0 to Infinity (MRT_{inf})

| | |
|-----------------|--|
| End point title | Single- and Repeat-Dose Pharmacokinetics - Mean Residence Time from Time 0 to Infinity (MRT _{inf}) |
|-----------------|--|

End point description:

MRT_{inf} is an average duration of the drug in the body from time zero to infinity, and is expressed in minutes. In the categories listed below, "N" signifies the number of subjects evaluable for the timepoint.

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

End point timeframe:

Weeks 1 and 27

| | | | | |
|--------------------------------------|-------------------|--|--|--|
| End point values | Idursulfase | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 26 ^[9] | | | |
| Units: minutes | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 1 (N=26) | 153 (± 96) | | | |
| Week 27 (N=18) | 127 (± 23) | | | |

Notes:

[9] - PK population with evaluable subjects for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Single- and Repeat-Dose Pharmacokinetics - Clearance (CL)

| | |
|-----------------|---|
| End point title | Single- and Repeat-Dose Pharmacokinetics - Clearance (CL) |
|-----------------|---|

End point description:

Clearance of a drug is a measure of the rate at which a drug is metabolized or eliminated by normal biological processes. In the categories listed below, "N" signifies the number of subjects evaluable for the timepoint.

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

End point timeframe:

Weeks 1 and 27

| End point values | Idursulfase | | | |
|--------------------------------------|--------------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 26 ^[10] | | | |
| Units: milliliter/minute/kilogram | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 1 (N=26) | 2.4 (± 0.7) | | | |
| Week 27 (N=18) | 4.7 (± 5) | | | |

Notes:

[10] - PK population with evaluable subjects for this endpoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Single- and Repeat-Dose Pharmacokinetics - Volume of Distribution at Steady State (Vss)

| | |
|-----------------|---|
| End point title | Single- and Repeat-Dose Pharmacokinetics - Volume of Distribution at Steady State (Vss) |
|-----------------|---|

End point description:

Volume of distribution is defined as the theoretical volume in which the total amount of drug would need to be uniformly distributed to produce the desired blood concentration of a drug. Vss is the apparent volume of distribution at steady-state. In the categories listed below, "N" signifies the number of subjects evaluable for the timepoint.

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

End point timeframe:

Weeks 1 and 27

| | | | | |
|--------------------------------------|--------------------|--|--|--|
| End point values | Idursulfase | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 26 ^[11] | | | |
| Units: milliliter per kilogram | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 1 (N=26) | 394 (± 423) | | | |
| Week 27 (N=18) | 551 (± 528) | | | |

Notes:

[11] - PK population with evaluable subjects for this endpoint.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the start of study treatment until 30 days after the last infusion of idursulfase

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 10.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|-------------|
| Reporting group title | Idursulfase |
|-----------------------|-------------|

Reporting group description:

Open-label treatment with idursulfase

| Serious adverse events | Idursulfase | | |
|--|------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 13 / 28 (46.43%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |
| Vascular disorders | | | |
| Haematoma | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Atonic seizures | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Microcytic anaemia | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Irritability | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Catheter site haematoma | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Oedema peripheral | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pyrexia | | | |
| subjects affected / exposed | 3 / 28 (10.71%) | | |
| occurrences causally related to treatment / all | 6 / 6 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Food poisoning | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypoxia | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bronchospasm | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|-----------------|--|--|
| Pulmonary hypertension | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory distress | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Skin hypertrophy | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Rash | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urticaria | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 2 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Muscle contracture | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Bronchopneumonia | | | |
| subjects affected / exposed | 3 / 28 (10.71%) | | |
| occurrences causally related to treatment / all | 0 / 3 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal infection | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Ear infection | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Otitis media | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Viral pharyngitis | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 3.57 %

| Non-serious adverse events | Idursulfase | | |
|---|-------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 28 / 28 (100.00%) | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Skin papilloma | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Vascular disorders | | | |
| Haematoma | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Hypertension | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Hyperaemia | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 2 | | |
| Haemorrhage | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| General disorders and administration site conditions | | | |
| Catheter site haemorrhage | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Chest pain | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Fatigue | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | | |
| occurrences (all) | 2 | | |
| Oedema peripheral | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Malaise | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 2 | | |

| | | | |
|---|------------------|--|--|
| Pyrexia | | | |
| subjects affected / exposed | 25 / 28 (89.29%) | | |
| occurrences (all) | 59 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Allergic cough | | | |
| subjects affected / exposed | 3 / 28 (10.71%) | | |
| occurrences (all) | 3 | | |
| Asthma | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | | |
| occurrences (all) | 2 | | |
| Choking | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Bronchospasm | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | | |
| occurrences (all) | 3 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Hypoxia | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Cough | | | |
| subjects affected / exposed | 16 / 28 (57.14%) | | |
| occurrences (all) | 45 | | |
| Nasal congestion | | | |
| subjects affected / exposed | 6 / 28 (21.43%) | | |
| occurrences (all) | 9 | | |
| Pharyngolaryngeal pain | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Lung infiltration | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Pulmonary hypertension | | | |

| | | | |
|-----------------------------|-----------------|--|--|
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Respiratory disorder | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Sleep apnoea syndrome | | | |
| subjects affected / exposed | 3 / 28 (10.71%) | | |
| occurrences (all) | 3 | | |
| Rhinorrhoea | | | |
| subjects affected / exposed | 3 / 28 (10.71%) | | |
| occurrences (all) | 4 | | |
| Psychiatric disorders | | | |
| Bipolar disorder | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Crying | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Insomnia | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Agitation | | | |
| subjects affected / exposed | 4 / 28 (14.29%) | | |
| occurrences (all) | 5 | | |
| Sleep disorder | | | |
| subjects affected / exposed | 3 / 28 (10.71%) | | |
| occurrences (all) | 3 | | |
| Learning disorder | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Investigations | | | |
| Cardiac murmur | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Hepatic enzyme abnormal | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 2 / 28 (7.14%) | | |
| occurrences (all) | 2 | | |
| Gamma-Glutamyltransferase increased | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Electrocardiogram repolarisation abnormality | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Monocyte count decreased | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Lymphocyte morphology abnormal | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Injury, poisoning and procedural complications | | | |
| Burns second degree | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Contusion | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Fall | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Head injury | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Mouth injury | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Limb injury | | | |

| | | | |
|--|-----------------|--|--|
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Procedural pain | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Sunburn | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Congenital, familial and genetic disorders | | | |
| Hip dysplasia | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Cardiac disorders | | | |
| Cardiomyopathy | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Aortic valve incompetence | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Cyanosis | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Right ventricular hypertrophy | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Left ventricular hypertrophy | | | |
| subjects affected / exposed | 4 / 28 (14.29%) | | |
| occurrences (all) | 4 | | |
| Sinus bradycardia | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Ventricular extrasystoles | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Nervous system disorders | | | |

| | | | |
|--------------------------------------|-----------------|--|--|
| Epilepsy | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Headache | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Hypoaesthesia | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Tremor | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | | |
| occurrences (all) | 2 | | |
| Somnolence | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Blood and lymphatic system disorders | | | |
| Eosinophilia | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Iron deficiency anaemia | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Splénomegaly | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Ear and labyrinth disorders | | | |
| Cerumen impaction | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 2 | | |
| Conductive deafness | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Deafness | | | |
| subjects affected / exposed | 4 / 28 (14.29%) | | |
| occurrences (all) | 4 | | |
| Ear pain | | | |

| | | | |
|--|-----------------------|--|--|
| subjects affected / exposed occurrences (all) | 1 / 28 (3.57%) 1 | | |
| Hearing impaired subjects affected / exposed occurrences (all) | 1 / 28 (3.57%) 1 | | |
| Hypoacusis subjects affected / exposed occurrences (all) | 2 / 28 (7.14%) 2 | | |
| Otorrhoea subjects affected / exposed occurrences (all) | 1 / 28 (3.57%) 1 | | |
| Eye disorders Conjunctivitis subjects affected / exposed occurrences (all) | 1 / 28 (3.57%) 1 | | |
| Hypermetropia subjects affected / exposed occurrences (all) | 2 / 28 (7.14%) 2 | | |
| Gastrointestinal disorders Abdominal pain subjects affected / exposed occurrences (all) | 1 / 28 (3.57%) 2 | | |
| Anal fissure subjects affected / exposed occurrences (all) | 1 / 28 (3.57%) 2 | | |
| Constipation subjects affected / exposed occurrences (all) | 2 / 28 (7.14%) 3 | | |
| Dental caries subjects affected / exposed occurrences (all) | 2 / 28 (7.14%) 2 | | |
| Diarrhoea subjects affected / exposed occurrences (all) | 7 / 28 (25.00%) 35 | | |
| Faeces hard | | | |

| | | | |
|--|------------------|--|--|
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 2 | | |
| Nausea | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 2 | | |
| Gingivitis | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Pruritus ani | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Stomatitis | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Toothache | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | | |
| occurrences (all) | 2 | | |
| Umbilical hernia | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Vomiting | | | |
| subjects affected / exposed | 10 / 28 (35.71%) | | |
| occurrences (all) | 12 | | |
| Skin and subcutaneous tissue disorders | | | |
| Dermatitis allergic | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 2 | | |
| Dermatitis | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Dermatitis atopic | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Heat rash | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | | |
| occurrences (all) | 4 | | |

| | | | |
|---|-----------------|--|--|
| Eczema | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | | |
| occurrences (all) | 2 | | |
| Dermatitis diaper | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | | |
| occurrences (all) | 3 | | |
| Erythema | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | | |
| occurrences (all) | 2 | | |
| Intertrigo | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Palmar-Plantar erythrodysaesthesia syndrome | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Pruritus | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Rash | | | |
| subjects affected / exposed | 6 / 28 (21.43%) | | |
| occurrences (all) | 11 | | |
| Petechiae | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | | |
| occurrences (all) | 2 | | |
| Rash generalised | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Rash maculo-papular | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | | |
| occurrences (all) | 2 | | |
| Rash papular | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | | |
| occurrences (all) | 2 | | |
| Skin hypopigmentation | | | |

| | | | |
|--|--|--|--|
| <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Skin lesion</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Urticaria</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Urticaria papular</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 28 (3.57%)</p> <p>1</p> <p>1 / 28 (3.57%)</p> <p>1</p> <p>3 / 28 (10.71%)</p> <p>4</p> <p>1 / 28 (3.57%)</p> <p>1</p> | | |
| <p>Renal and urinary disorders</p> <p>Enuresis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 28 (3.57%)</p> <p>1</p> | | |
| <p>Musculoskeletal and connective tissue disorders</p> <p>Lordosis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Muscle contracture</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Arthralgia</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> | <p>1 / 28 (3.57%)</p> <p>1</p> <p>1 / 28 (3.57%)</p> <p>1</p> <p>1 / 28 (3.57%)</p> <p>2</p> | | |
| <p>Infections and infestations</p> <p>Abscess limb</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Body tinea</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Bronchitis</p> <p>subjects affected / exposed</p> <p>occurrences (all)</p> <p>Bronchopneumonia</p> | <p>1 / 28 (3.57%)</p> <p>1</p> <p>1 / 28 (3.57%)</p> <p>1</p> <p>4 / 28 (14.29%)</p> <p>4</p> | | |

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|-----------------------------|-----------------|--|--|
| subjects affected / exposed | 3 / 28 (10.71%) | | |
| occurrences (all) | 4 | | |
| Catheter site infection | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Candidiasis | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Ear infection | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | | |
| occurrences (all) | 2 | | |
| Gastrointestinal infection | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | | |
| occurrences (all) | 2 | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 6 / 28 (21.43%) | | |
| occurrences (all) | 7 | | |
| Herpes virus infection | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | | |
| occurrences (all) | 2 | | |
| Influenza | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | | |
| occurrences (all) | 2 | | |
| Herpes zoster | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Lice infestation | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Laryngitis | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | | |
| occurrences (all) | 2 | | |
| Nasopharyngitis | | | |

| | | | |
|-----------------------------|------------------|--|--|
| subjects affected / exposed | 2 / 28 (7.14%) | | |
| occurrences (all) | 2 | | |
| Oral candidiasis | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Otitis externa | | | |
| subjects affected / exposed | 3 / 28 (10.71%) | | |
| occurrences (all) | 5 | | |
| Otitis media acute | | | |
| subjects affected / exposed | 7 / 28 (25.00%) | | |
| occurrences (all) | 10 | | |
| Otitis media | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | | |
| occurrences (all) | 3 | | |
| Pharyngitis | | | |
| subjects affected / exposed | 7 / 28 (25.00%) | | |
| occurrences (all) | 18 | | |
| Rash pustular | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Otitis media chronic | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Respiratory tract infection | | | |
| subjects affected / exposed | 12 / 28 (42.86%) | | |
| occurrences (all) | 36 | | |
| Pneumonia | | | |
| subjects affected / exposed | 3 / 28 (10.71%) | | |
| occurrences (all) | 3 | | |
| Rhinitis | | | |
| subjects affected / exposed | 11 / 28 (39.29%) | | |
| occurrences (all) | 20 | | |
| Sinusitis | | | |
| subjects affected / exposed | 5 / 28 (17.86%) | | |
| occurrences (all) | 6 | | |
| Tinea versicolour | | | |

| | | | |
|---|------------------|--|--|
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Tonsillitis bacterial | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 2 | | |
| Tonsillitis | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | | |
| occurrences (all) | 2 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 18 / 28 (64.29%) | | |
| occurrences (all) | 42 | | |
| Viral diarrhoea | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 2 | | |
| Upper respiratory tract infection bacterial | | | |
| subjects affected / exposed | 6 / 28 (21.43%) | | |
| occurrences (all) | 13 | | |
| Varicella | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Viral pharyngitis | | | |
| subjects affected / exposed | 2 / 28 (7.14%) | | |
| occurrences (all) | 2 | | |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 9 / 28 (32.14%) | | |
| occurrences (all) | 17 | | |
| Viral infection | | | |
| subjects affected / exposed | 3 / 28 (10.71%) | | |
| occurrences (all) | 4 | | |
| Metabolism and nutrition disorders | | | |
| Obesity | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Hypercalcaemia | | | |

| | | | |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |
| Hyperuricaemia | | | |
| subjects affected / exposed | 1 / 28 (3.57%) | | |
| occurrences (all) | 1 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported