# EU Clinical Trials Register

## Clinical trial results:

## A Phase 3, Open Label, Switch Over Study to Assess the Safety, Efficacy and Pharmacokinetics of pegunigalsidase alfa (PRX-102) 2 mg/kg Administered by Intravenous Infusion Every 4 Weeks for 52 weeks in Patients with Fabry Disease Currently Treated with Enzyme Replacement Therapy; Fabrazyme® (agalsidase beta) or Replagal™ (agalsidase alfa)

### Summary

| | |
|---|---|
| EudraCT number | 2017-001528-23 |
| Trial protocol | GB BE ES CZ DK IT |
| Global end of trial date | 01 August 2020 |

### Results information

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 06 April 2022 |
| First version publication date | 06 April 2022 |

### Trial information

#### Trial identification

| | |
|---|---|
| Sponsor protocol code | PB-102-F50 |

#### Additional study identifiers

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT03180840 |
| WHO universal trial number (UTN) | - |

Notes:

#### Sponsors

| | |
|---|---|
| Sponsor organisation name | Protalix Ltd. |
| Sponsor organisation address | 2 Snunit Street, Carmiel, Israel, 2161401 |
| Public contact | Raul Chertkoff, Protalix Ltd., +972 4-902-8100, raul@protalix.com |
| Scientific contact | Sari Alon, Protalix Ltd., +972 4-902-8100, sari@protalix.com |

Notes:

#### Paediatric regulatory details

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

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 03 November 2021 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 01 August 2020 |
| Global end of trial reached? | Yes |
| Global end of trial date | 01 August 2020 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the safety, efficacy and pharmacokinetics of pegunigalsidase alfa (PRX-102) at a dosing regimen of 2.0 mg/kg every 4 weeks in patients with Fabry disease currently treated with currently commercially available ERT (agalsidase alfa or agalsidase beta).

Protection of trial subjects:

The first administrations of pegunigalsidase alfa were performed under controlled conditions at the investigational site.
Premedication, if used for the patient's agalsidase alfa or agalsidase beta infusions before study entry, was continued  for the first infusion with pegunigalsidase alfa, and then gradually tapered down at the Investigator's discretion and according to the patient's tolerability during the next infusions.
Patients were allowed to receive the infusions in a home care set-up if the Investigator and Sponsor Medical Director/Monitor agreed that it was safe to do so and once the patient was clinically stable and there were no additional changes to premedication, infusion rate or observation time.
In cases of clear clinical deterioration, the treatment could have been changed to 1.0 mg/kg every 2 weeks at the Investigator's discretion and following discussion with the Sponsor Medical Director/Monitor.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 10 July 2017 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety, Efficacy, Ethical reason |
| Long term follow-up duration | 4 Years |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | United States: 18 |
| Country: Number of subjects enrolled | Norway: 1 |
| Country: Number of subjects enrolled | United Kingdom: 2 |
| Country: Number of subjects enrolled | Belgium: 2 |
| Country: Number of subjects enrolled | Czechia: 3 |
| Country: Number of subjects enrolled | Denmark: 1 |
| Country: Number of subjects enrolled | Italy: 3 |
| Worldwide total number of subjects | 30 |
| EEA total number of subjects | 10 |

Notes:

## Subjects enrolled per age group

| | |
|---|---|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 30 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details:

Patients who were treated with agalsidase beta or agalsidase alfa for at least 3 years, and have been on a stable dose (> 80% labelled dose/kg) for at least 6 months.

### Pre-assignment

Screening details:

A total of 30 patients (24 males and 6 females) were enrolled and switched from agalsidase alfa or agalsidase beta to pegunigalsidase alfa over a 52-week period, of whom 29 patients (23 males and 6 females) completed the study.

### Pre-assignment period milestones

| | |
|---|---|
| Number of subjects started | 30 |
| Number of subjects completed | 30 |

### Period 1

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

Blinding implementation details:

Open Label

### Arms

| Arm title | pegunigalsidase alfa |
|---|---|

Arm description:

pegunigalsidase alfa 2.0 mg/kg every 4 weeks for 12 months

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | pegunigalsidase alfa |
| Investigational medicinal product code | |
| Other name | PRX-102 |
| Pharmaceutical forms | Concentrate for solution for infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

2.0 mg/kg administered by intravenous (IV) infusion every 4 weeks  for 12 months

| Number of subjects in period 1 | pegunigalsidase alfa |
|---|---|
| Started | 30 |
| Completed | 29 |
| Not completed | 1 |
|    Consent withdrawn by subject | 1 |

## Baseline characteristics

### Reporting groups

| Reporting group title | Overall trial |
| --- | --- |
| Reporting group description: | |
| All treated patients | |

| Reporting group values | Overall trial | Total | |
| --- | --- | --- | --- |
| Number of subjects | 30 | 30 | |
| Age categorical | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 30 | 30 | |
| Age continuous | | | |
| Units: years | | | |
| arithmetic mean | 40.5 | | |
| standard deviation | ± 11.3 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 6 | 6 | |
| Male | 24 | 24 | |
| Previous ERT | | | |
| Previously treated with agalsidase beta or anti-agalsidase alfa | | | |
| Units: Subjects | | | |
| Agalsidase alfa | 7 | 7 | |
| Agalsidase beta | 23 | 23 | |

### Subject analysis sets

| Subject analysis set title | Safety population |
| --- | --- |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| Safety population, defined as all patients who received at least one dose (partial or complete) of pegunigalsidase alfa in the study | |
| Subject analysis set title | Efficacy population |
| Subject analysis set type | Per protocol |
| Subject analysis set description: | |
| Efficacy population, defined as all patients who received any dose of pegunigalsidase alfa 2.0 mg/kg in this study and who had at least one post-baseline visit with an efficacy evaluation | |
| Subject analysis set title | Male |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| Male subjects from safety population | |
| Subject analysis set title | Female |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| Female subjects from safety population | |

| Reporting group values | Safety population | Efficacy population | Male |
|---|---|---|---|
| **Number of subjects** | 30 | 29 | 24 |
| Age categorical<br>Units: Subjects | | | |
| Adults (18-64 years) | 30 | 29 | 24 |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 40.5 | | 39.3 |
| standard deviation | ± 11.3 | ± | ± 12.2 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 6 | 6 | 6 |
| Male | 24 | 23 | 24 |
| Previous ERT | | | |
| Previously treated with agalsidase beta or anti-agalsidase alfa | | | |
| Units: Subjects | | | |
| Agalsidase alfa | 7 | | 5 |
| Agalsidase beta | 23 | | 19 |

| Reporting group values | Female | | |
|---|---|---|---|
| **Number of subjects** | 6 | | |
| Age categorical<br>Units: Subjects | | | |
| Adults (18-64 years) | 6 | | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 45.2 | | |
| standard deviation | ± 5.3 | | |
| Gender categorical<br>Units: Subjects | | | |
| Female | 6 | | |
| Male | 24 | | |
| Previous ERT | | | |
| Previously treated with agalsidase beta or anti-agalsidase alfa | | | |
| Units: Subjects | | | |
| Agalsidase alfa | 2 | | |
| Agalsidase beta | 4 | | |

## End points

### End points reporting groups

| Reporting group title | pegunigalsidase alfa |
|---|---|
| Reporting group description: | |
| pegunigalsidase alfa 2.0 mg/kg every 4 weeks for 12 months | |
| Subject analysis set title | Safety population |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: | |
| Safety population, defined as all patients who received at least one dose (partial or complete) of pegunigalsidase alfa in the study | |
| Subject analysis set title | Efficacy population |
| Subject analysis set type | Per protocol |
| Subject analysis set description: | |
| Efficacy population, defined as all patients who received any dose of pegunigalsidase alfa 2.0 mg/kg in this study and who had at least one post-baseline visit with an efficacy evaluation | |
| Subject analysis set title | Male |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| Male subjects from safety population | |
| Subject analysis set title | Female |
| Subject analysis set type | Sub-group analysis |
| Subject analysis set description: | |
| Female subjects from safety population | |

### Primary: Number of participants experiencing adverse events (AEs)

| End point title | Number of participants experiencing adverse events (AEs)[1] |
|---|---|
| End point description: | |
| Results represent the number of treatment-emergent adverse events (TEAE) that were considered possibly, probably, or definitely related to treatment | |
| End point type | Primary |
| End point timeframe: | |
| 12 months | |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical analysis was specified for this study, the data was summarized using descriptive statistics.

| **End point values** | Safety population | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 30 | | | |
| Units: subjects | | | | |
| At least 1 TEAE | 27 | | | |
| At least 1 mild or moderate TEAE | 26 | | | |
| At least 1 severe TEAE | 2 | | | |
| At least 1 serious TEAE | 2 | | | |
| At least 1 non-serious TEAE | 26 | | | |
| At least 1 related TEAE | 9 | | | |
| At least 1 related mild or moderate TEAE | 9 | | | |
| At least 1 related severe TEAE | 0 | | | |

| | | | | |
|---|---|---|---|---|
| At least 1 related serious TEAE | 0 | | | |
| At least 1 TEAE leading to withdrawal | 0 | | | |
| At least 1 TEAE leading to death | 0 | | | |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Estimated Glomerular Filtration Rate (eGFR)

| End point title | Estimated Glomerular Filtration Rate (eGFR) |
|---|---|

End point description:

eGFR was calculated based on the serum creatinine values according to the CKD-EPI formula. The absolute change in eGFR from baseline measurement at visit 1 to last measurement at Month 12 was summarized using descriptive statistics.

| End point type | Other pre-specified |
|---|---|

End point timeframe:

12 Months

| **End point values** | Efficacy population | Male | Female | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 29 | 23 | 6 | |
| Units: mL/min/1.73 m^2 | | | | |
| arithmetic mean (standard error) | | | | |
| Baseline | 99.44 (± 4.15) | 100.68 (± 4.96) | 94.69 (± 6.76) | |
| Month 12 | 100.65 (± 3.14) | 103.24 (± 3.46) | 91.15 (± 6.39) | |
| Change from Baseline to Month 12 | -1.27 (± 1.39) | -0.64 (± 1.57) | -3.54 (± 3.12) | |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Plasma Lyso-Gb3

| End point title | Plasma Lyso-Gb3 |
|---|---|

End point description:

Globotriaosylsphingosine (Lyso-Gb3) is Fabry disease specific biomarker that can assess treatment outcome.

| End point type | Other pre-specified |
|---|---|

End point timeframe:

12 Month

| End point values | Efficacy population | Male | Female | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 29 | 23 | 6 | |
| Units: nM | | | | |
| arithmetic mean (standard error) | | | | |
| Baseline | 19.36 (± 3.35) | 23.27 (± 3.82) | 4.35 (± 1.00) | |
| Month 12 | 22.23 (± 3.60) | 27.05 (± 4.00) | 4.52 (± 1.10) | |
| Change from Baseline to Month 12 | 3.01 (± 0.94) | 3.79 (± 1.14) | 0.17 (± 0.34) | |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Quality of life by EQ VAS

| End point title | Quality of life by EQ VAS |
|---|---|
| End point description: | |

The EQ VAS, of the EQ 5D 5L questionnaire, records the subject's self-rated health on a vertical, visual analogue scale where the endpoints are labelled 'Best imaginable health state' (score "100") and 'Worst imaginable health state' (score "0").

| End point type | Other pre-specified |
|---|---|
| End point timeframe: | |

12 Months

| End point values | Efficacy population | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 29 | | | |
| Units: Score | | | | |
| arithmetic mean (standard error) | | | | |
| Baseline | 78.3 (± 3.1) | | | |
| Month 12 | 82.1 (± 2.9) | | | |
| Change from Baseline to Month 12 | 3.0 (± 2.2) | | | |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Pharmacokinetics – Cmax

| End point title | Pharmacokinetics – Cmax |
|---|---|
| End point description: | |

Pharmacokinetic (PK) parameters were derived from the plasma concentration versus time profiles.
Cmax is the maximal plasma concentration of a drug after administration.
Results reported represent the values following a single dosing of the study drug.

| End point type | Other pre-specified |
|---|---|

End point timeframe:

PK parameters were determined on Day 1, Month 9 or 11, and month 12.

| End point values | Safety population | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 30 | | | |
| Units: ng/ml | | | | |
| arithmetic mean (standard deviation) | | | | |
| Pharmacokinetics | 35876.7 (± 11942.2) | | | |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Pharmacokinetics – AUC

| End point title | Pharmacokinetics – AUC |
|---|---|

End point description:

PK parameters were derived from the plasma concentration versus time profiles.
AUC0-∞ is the area under the plasma concentration curve from 0 hours to infinity. Results reported represent the values following a single dosing of the study drug.

| End point type | Other pre-specified |
|---|---|

End point timeframe:

PK parameters were determined on Day 1, Month 9 or 11 and Month 12.

| End point values | Safety population | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 30 | | | |
| Units: ng*hr/ml | | | | |
| arithmetic mean (standard deviation) | | | | |
| Pharmacokinetics | 1797464.1 (± 822632.4) | | | |

## Statistical analyses

No statistical analyses for this end point

## Other pre-specified: Pharmacokinetics - Terminal Half Life

| End point title | Pharmacokinetics - Terminal Half Life |
|---|---|

End point description:

PK parameters were derived from the plasma concentration versus time profiles.
t1/2 = half life.
Results reported represent the values following a single dosing of the study drug.

| End point type | Other pre-specified |
|---|---|

End point timeframe:

PK parameters were determined on Day 1, Month 9 or 11 and Month 12.

| **End point values** | Safety population | | | |
|---|---|---|---|---|
| Subject group type | Subject analysis set | | | |
| Number of subjects analysed | 30 | | | |
| Units: hour | | | | |
| arithmetic mean (standard deviation) | | | | |
| Pharmacokinetics | 100.1 (± 58.3) | | | |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

AEs were collected from the start of treatment until 30 days following the final study dose.

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

### Dictionary used

| Dictionary name | MedDRA |
|---|---|
| Dictionary version | 19 |

### Reporting groups

| Reporting group title | All Patients |
|---|---|

Reporting group description:

Analysis of AEs was performed on TEAEs, defined as AEs occurring after the start of the first infusion with pegunigalsidase alfa.

| **Serious adverse events** | All Patients | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Injury, poisoning and procedural complications | | | |
| Overdose | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Road traffic accident | | | |
| subjects affected / exposed | 1 / 30 (3.33%) | | |
| 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** | All Patients | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 27 / 30 (90.00%) | | |
| Injury, poisoning and procedural complications | | | |

| | | | |
|---|---|---|---|
| Infusion related reaction | | | |
| subjects affected / exposed | 5 / 30 (16.67%) | | |
| occurrences (all) | 17 | | |
| Contusion | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 2 | | |
| **Nervous system disorders** | | | |
| Headache | | | |
| subjects affected / exposed | 3 / 30 (10.00%) | | |
| occurrences (all) | 4 | | |
| Paraesthesia | | | |
| subjects affected / exposed | 3 / 30 (10.00%) | | |
| occurrences (all) | 3 | | |
| Neuralgia | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 2 | | |
| **General disorders and administration site conditions** | | | |
| Pain | | | |
| subjects affected / exposed | 3 / 30 (10.00%) | | |
| occurrences (all) | 9 | | |
| Fatigue | | | |
| subjects affected / exposed | 5 / 30 (16.67%) | | |
| occurrences (all) | 6 | | |
| Chest discomfort | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 2 | | |
| Pyrexia | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 2 | | |
| **Ear and labyrinth disorders** | | | |
| Ear pain | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 2 | | |
| Hypoacusis | | | |
| subjects affected / exposed | 2 / 30 (6.67%) | | |
| occurrences (all) | 2 | | |

| | | | |
|---|---|---|---|
| **Gastrointestinal disorders** | | | |
|   Diarrhoea | | | |
|     subjects affected / exposed | 3 / 30 (10.00%) | | |
|     occurrences (all) | 4 | | |
|   Nausea | | | |
|     subjects affected / exposed | 4 / 30 (13.33%) | | |
|     occurrences (all) | 4 | | |
|   Gastrooesophageal reflux disease | | | |
|     subjects affected / exposed | 2 / 30 (6.67%) | | |
|     occurrences (all) | 2 | | |
|   Vomiting | | | |
|     subjects affected / exposed | 2 / 30 (6.67%) | | |
|     occurrences (all) | 2 | | |
| **Respiratory, thoracic and mediastinal disorders** | | | |
|   Cough | | | |
|     subjects affected / exposed | 4 / 30 (13.33%) | | |
|     occurrences (all) | 4 | | |
|   Oropharyngeal pain | | | |
|     subjects affected / exposed | 3 / 30 (10.00%) | | |
|     occurrences (all) | 4 | | |
| **Psychiatric disorders** | | | |
|   Anxiety | | | |
|     subjects affected / exposed | 2 / 30 (6.67%) | | |
|     occurrences (all) | 2 | | |
| **Musculoskeletal and connective tissue disorders** | | | |
|   Pain in extremity | | | |
|     subjects affected / exposed | 3 / 30 (10.00%) | | |
|     occurrences (all) | 4 | | |
|   Myalgia | | | |
|     subjects affected / exposed | 2 / 30 (6.67%) | | |
|     occurrences (all) | 2 | | |
| **Infections and infestations** | | | |
|   Nasopharyngitis | | | |
|     subjects affected / exposed | 6 / 30 (20.00%) | | |
|     occurrences (all) | 7 | | |
|   Gastroenteritis | | | |

| | |
|---|---|
| subjects affected / exposed | 2 / 30 (6.67%) |
| occurrences (all) | 4 |
| **Sinusitis** | |
| subjects affected / exposed | 3 / 30 (10.00%) |
| occurrences (all) | 3 |
| **Upper respiratory tract infection** | |
| subjects affected / exposed | 2 / 30 (6.67%) |
| occurrences (all) | 3 |
| **Viral infection** | |
| subjects affected / exposed | 3 / 30 (10.00%) |
| occurrences (all) | 3 |
| **Gastroenteritis viral** | |
| subjects affected / exposed | 2 / 30 (6.67%) |
| occurrences (all) | 2 |
| **Influenza** | |
| subjects affected / exposed | 2 / 30 (6.67%) |
| occurrences (all) | 2 |
| **Pharyngitis streptococcal** | |
| subjects affected / exposed | 2 / 30 (6.67%) |
| occurrences (all) | 2 |

## 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

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

| |
|---|
| Small number of subjects |

Notes: