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 Units: Subjects			
Adults (18-64 years)	30	29	24
Age continuous Units: years			
arithmetic mean	40.5		39.3
standard deviation	± 11.3	±	± 12.2
Gender categorical 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 Units: Subjects			
Adults (18-64 years)	6		
Age continuous Units: years			
arithmetic mean	45.2		
standard deviation	± 5.3		
Gender categorical 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 occurrences (all) Contusion subjects affected / exposed occurrences (all)	5 / 30 (16.67%) 17 2 / 30 (6.67%) 2		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Paraesthesia subjects affected / exposed occurrences (all) Neuralgia subjects affected / exposed occurrences (all)	3 / 30 (10.00%) 4 3 / 30 (10.00%) 3 2 / 30 (6.67%) 2		
General disorders and administration site conditions Pain subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) Chest discomfort subjects affected / exposed occurrences (all) Pyrexia subjects affected / exposed occurrences (all)	3 / 30 (10.00%) 9 5 / 30 (16.67%) 6 2 / 30 (6.67%) 2 2 / 30 (6.67%) 2		
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all) Hypoacusis subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 2 2 / 30 (6.67%) 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: