Open Label Extension Study to Evaluate the Long-Term Safety and Efficacy of Pegunigalsidase Alfa (PRX-102) in Patients with Fabry Disease

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To evaluate the ongoing safety, tolerability, and efficacy parameters of pegunigalsidase alfa in adult Fabry patients who have successfully completed studies PB-102-F20 and PB-102-F30, or completed at least 48 months in study PB-102-F03.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Metabolic and nutritional disorders congenital
Study type	Interventional

Summary

ID

NL-OMON52441

Source
ToetsingOnline

Brief title
PB-102-F60/Brilliance Study

Condition

- Metabolic and nutritional disorders congenital

Synonym
Fabry disease, lysosomal storage disease

Research involving
Human

Sponsors and support

Primary sponsor: Chiesi Farmaceutici S.p.A

Source(s) of monetary or material Support: The pharmaceutical industry

Intervention

Keyword: Efficacy, Pegunigalsidase alfa, PRX-102, Safety

Outcome measures

Primary outcome

SAFETY ENDPOINTS:

Changes from baseline in:

• Clinical laboratory tests

• Physical examination

• Assessment of the injection site

• Electrocardiography (ECG)

• Brain MRI

• Treatment-emergent adverse events (TEAE)

• Ability to taper off infusion pre-medication at the start of the study

• Requirement for use of pre-medication overall to manage infusion reactions

• Treatment-emergent anti-pegunigalsidase alfa antibodies

Secondary outcome

EFFICACY ENDPOINTS:

• Estimated glomerular filtration rate (eGFRCKD-EPI)

• Left Ventricular Mass Index (g/m2) by magnetic resonance imaging (MRI)

• Plasma Lyso-Gb3

• Plasma Gb3 concentration

• Protein/Creatinine ratio, spot urine test (UPCR)

• Frequency of pain medication use

• Exercise tolerance (Stress Test)

• Short Form Brief Pain Inventory (BPI)

• Mainz Severity Score Index (MSSI)

• Quality of life (EQ-5D-5L)

• Fabry disease clinical events

Study description

Background summary

Fabry disease is a progressive lysosomal storage disease that is seriously debilitating and ultimately life-threatening. It is caused by X-linked deficiency of the enzyme α-galactosidase A (α-GAL) and affects both males and females. The disease is characterized by subnormal or absent activity of α-GAL. Clinical onset of the disease typically occurs during childhood or adolescence (Schaefer et al., 2009) and will progress to end-stage renal disease (ESRD), cardiac complications, and cerebrovascular problems in the fourth or fifth decade of life (Wilcox et al., 2008). Although Fabry disease is a X-linked disorder, females are also affected and develop manifestations of the disease due to lack of cross-correction between cells with normal α-GAL activity (mutated X chromosome is inactivated) and cells with enzyme deficiency (non-mutated X chromosome is inactivated). The clinical abnormalities in females are more variable, and of later onset compared to males).
Fabry disease is regarded as a rare disease and it is estimated that 1 in 40,000 males has the disease, whereas the
estimated prevalence in the general population is 1 in 117,000.
Protalix has developed PRX-102, a chemically modified recombinant human alpha-GAL-A expressed in plant cell
culture. As a result of this modification, PRX-102 exhibits more stabilized homo dimer with active enzyme over longer
period, extended circulation residence time and enhanced bioavailability of the enzyme relative to the commercial drug.
Therefore, PRX-102 provides continuous presence of enzyme over the 2 week dosing interval.

Study objective

To evaluate the ongoing safety, tolerability, and efficacy parameters of pegunigalsidase alfa in adult Fabry patients who have successfully completed studies PB-102-F20 and PB-102-F30, or completed at least 48 months in study

PB-102-F03.

Study design

This will be an open-label, multicenter study of 1 mg/kg of pegunigalsidase alfa intravenous infusion every 2 weeks (±3 days) to evaluate the safety, tolerability, and efficacy of pegunigalsidase alfa in adult Fabry patients (>=18 years of age).
The duration of treatment will up to 60 months or until pegunigalsidase alfa is available to the patient, or at the discretion of the Sponsor.
The disease parameters that were evaluated during study PB-102-F20, PB-102-F30 and PB-102-F03 will continue to be assessed in this extension protocol (Study PB-102-F60).

Intervention

All patients who completed study PB-102-F20 will be treated in study PB-102-F60 with pegunigalsidase alfa 1 mg/kg every other week. Study PB-102-F20 is an ongoing double-blind study in which up to 26 patients are treated with agalsidase beta. To maintain the blinding of study PB-102-F20, the first infusion in PB-102-F60 of these patients will be administered intravenously over 3 hours with 2 hours post dosing clinical observation. Subsequent infusions will be managed according to Appendix 7, primary investigator (PI) evaluation, and Medical Director approval. Premedication, if used in PB-102-F20 infusions, will be continued with the first infusion in PB-102-F60 and then tapered down at the PI*s discretion pending the patient tolerability and according to Appendix 7.
The patient will be able to return to the previous established treatment format, whether home infusion or through a predefined infusion center, once the PI and Sponsor Medical Director agree that it is safe to do so.
Patients who completed the PB-102-F30 or PB-102-F03 study can continue the infusions at the same duration achieved in the previous study but not less than 60 minutes, with post dosing observation time of an additional 60 minutes and the same premedication if used.
Reduction of the infusion time from 90 minutes to 60 minutes will be done in a step-wise manner pending tolerability and after medical monitor approval.

Study burden and risks

Pegunigalsidase alfa has been given to 100 people for a duration of more than a year, but the specific side effects are not yet well known. The safety profile of pegunigalsidase alfa however does not seem very different from other Enzyme Replacement Therapies used to treat Fabry disease.
It is possible that the symptoms will not improve during the study or may even worsen. Please see the Investigators
Brochure and/or Informed Consent form for an overview of all possible side

effects.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Completion of study PB-102-F20 or PB-102-F30, or completed at least 48 months in study PB-102-F03.
2. The patient signs informed consent
3. Female patients and male patients whose co-partners are of childbearing potential agree to use a medically ccepted, highly effective method of contraception. These include combined (estrogen- and progestogen-containing) hormonal contraception associated with inhibition of ovulation (oral, intravaginal, or transdermal) supplemented with a barrier method (preferably male condom), progestogen-only hormonal contraception associated with inhibition of ovulation (oral,

injectable, or implantable) supplemented with a barrier method (preferably male condom), intrauterine device (IUD), intrauterine hormone-releasing system (IUS), bilateral tubal occlusion,
vasectomised partner, or sexual abstinence. Contraception should be used for 2 weeks after treatment termination.

Exclusion criteria

Presence of any medical, emotional, behavioral or psychological condition that, in the judgment of the Investigator would interfere with patient compliance with the requirements of the study.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	29-10-2019
Enrollment:	5
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	NA
Generic name:	Pegunigalsidase alfa

Ethics review

Approved WMO Date:	13-03-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-06-2019
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-10-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-04-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-06-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-12-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-01-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-11-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-04-2022

Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-06-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-08-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-12-2022
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl
Approved WMO Date:	12-05-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl
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Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl
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Application type:	Amendment
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Approved WMO

Date:	17-06-2024
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2018-001148-67-NL
ClinicalTrials.gov	NCT03566017
CCMO	NL68273.018.19