An Open-Label, Dose Escalation and Double-Masked, Randomized, Controlled Study to Evaluate the Safety and Tolerability of Sepofarsen in Pediatric Subjects <8 Years of Age with Leber Congenital Amaurosis Type 10 (LCA10) due to the c.2991 +1655A>G (p.Cys998X) mutation

Published: 24-07-2020
Last updated: 09-04-2024

Primary: To evaluate safety and tolerability of sepofarsen in subjects with LCA10

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cytoplasmic disorders congenital
Study type	Interventional

Summary

ID

NL-OMON55235

Source
ToetsingOnline

Brief title
PQ-110-005

Condition

- Cytoplasmic disorders congenital

Synonym
Leber Congenital Amaurosis. Leber's Disease

Research involving
Human

Sponsors and support

Primary sponsor: ProQR Therapeutics
Source(s) of monetary or material Support: ProQR Therapeutics

Intervention

Keyword: Leber Congenital Amaurosis (LCA), pediatric, sepofarsen

Outcome measures

Primary outcome

• Incidence and severity of ocular adverse events (AEs)

• Incidence and severity of non-ocular AEs.

Secondary outcome

Change from baseline to Month 12 in:

• BCVA

• Retinal sensitivity measured by FST (white, red, and blue)

Study description

Background summary

Leber congenital amaurosis caused by mutations in the CEP290 gene (LCA10) is a severe inherited retinal degenerative disease resulting in blindness. In patients with LCA10 due to the c.2991+1655A>G (p.Cys998X) mutation, visual symptoms are usually detectable before 1 year of age. Patients show severe vision impairment from an early age and in some cases further slowly progressing loss of remaining vision. There are currently no approved therapies for the treatment of LCA10 and therefore a high unmet medical need exists. Available safety and efficacy data from trial PQ 110-001 (NCT03140969), a Phase 1b/2, open-label, multiple-dose, dose-escalation first-in-human trial to evaluate the safety and tolerability of sepofarsen in subjects with LCA10 due to the c.2991+1655A>G (p.Cys998X) mutation from the age of 8 years and older, support the therapeutic potential observed in the nonclinical studies. A

pivotal Phase 2/3 trial in subjects of age 8 years and older is ongoing (PQ-110-003). As the disease onset of LCA10 is in infancy and early childhood, patients could potentially benefit from earlier initiation of treatment with sepofarsen. This current trial PQ-110-005 will include subjects younger than 8 years of age to extend the data on safety and tolerability in this age group. considering the individual subject*s response and the available safety information.

Study objective

Primary: To evaluate safety and tolerability of sepofarsen in subjects with LCA10 <8 years of age.
Secondary: To evaluate the effect of sepofarsen on structural and functional ophthalmic outcome measures.

Study design

PQ-110-005 is An Open-Label, Dose Escalation and Double-Masked, Randomized, Controlled Study to Evaluate the Safety and Tolerability of Sepofarsen in Pediatric Subjects <8 Years of Age with Leber Congenital Amaurosis Type 10 (LCA10) due to the c.2991 +1655A>G (p.Cys998X) mutation.
Dose cohorts are planned using a staggered dose escalation design. The study consists of two parts: an open-label dose escalation part, followed by a double-masked randomized part. The current open label part will evaluate 3 dose levels (cohorts). In the double-masked, randomized, controlled part of the study, subjects will be randomized to 2 dose levels (cohorts). Subjects will receive an unilateral IVT injection on Day 1. Thereafter a 6-monthly dosing schedule is planned, considering the individual subject*s response.

Intervention

The study consists of two parts: an open-label dose escalation part, followed by a double-masked randomized part. The current open label part will evaluate 3 dose levels (cohorts). In the double-masked, randomized, controlled part of the study, subjects will be randomized to 2 dose levels (cohorts). Subjects will receive an unilateral IVT injection on Day 1. Thereafter a 6-monthly dosing schedule is planned, considering the individual subject*s response and the available safety information.

Study burden and risks

In total there are 15 visits to the research center, with 4 telephone visits in addition. The study drug will be administered via intravitreal injection. In addition to the administration of the study drug, various tests are performed.

Subjects will receive a unilateral IVT injection of sepofarsen on Day 1.

Thereafter a 6-monthly dosing schedule is planned, considering the individual subject*s response. The decision for any re-dosing and the decision on dose level will be decided for each subject individually based on the ongoing data monitoring by Investigator and Medical Monitor and, if appropriate, the DMC. The dose level for re-dosing may therefore be different from the initial (dose escalation phase) dose level.

Duration of Subject Participation is up to 27 months (up to 12 weeks screening; 24 months follow-up post first dose)

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

1. Male or female child, <8 years of age at Screening
2. A clinical diagnosis of LCA and a molecular diagnosis of homozygosity or

compound heterozygosity for the c.2991+1655A>G mutation in the CEP290 gene, based on genotyping analysis at Screening. Historic genotyping results from a certified laboratory are acceptable with Sponsor approval.
3. BCVA equal to or better than Light Perception, and equal to or worse than approximate Snellen equivalent 20/50 in the treatment eye.
4. Clear ocular media and adequate pupillary dilation to permit good quality retinal imaging, as determined by the Investigator.

Exclusion criteria

1. Presence of pathogenic mutations in genes associated with other recessive, dominant or X-linked inherited retinal degenerative diseases or syndromes based on genetic analysis.
2. Presence of any significant ocular or non-ocular disease/disorder (including medication abnormalities) which may either put the subject at risk because of participation in the trial, may influence the results of the trial, or the subject*s ability to participate in the trial.
3. Receipt within 1 month prior to Screening of any intraocular or periocular surgery (including refractive surgery), or an IVT injection or planned intraocular surgery or procedure during the course of the trial.
4. Current treatment or treatment within the past 3 months or planned treatment with drugs known to be toxic to the lens, retina, or the optic nerve
5. Use of any investigational drug or device within 3 months or 5 half-lives of Day 1, whichever is longer, or plans to participate in another study of a drug or device during the trial period.
6. Any prior receipt of genetic or stem-cell therapy for ocular or non-ocular disease.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Double blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	23-03-2021
Enrollment:	3
Type:	Actual

Ethics review

Approved WMO Date:	24-07-2020
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	16-10-2020
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	26-03-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	16-04-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	24-03-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	04-04-2022

Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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	EUCTR2020-000535-45-NL
CCMO	NL74636.000.20

Study results

Date completed:	18-10-2022
Actual enrolment:	3

Summary results
Trial is onging in other countries