Natural History Study of CEP290-Related Retinal Degeneration

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Ethical review	Approved WMO
Status	Completed
Health condition type	Retina, choroid and vitreous haemorrhages and vascular disorders
Study type	Observational non invasive

Summary

ID

NL-OMON55731

Source
ToetsingOnline

Brief title
EDIT-NHS01

Condition

- Retina, choroid and vitreous haemorrhages and vascular disorders

Synonym
CEP290 mutation, Retinal Degeneration

Research involving
Human

Sponsors and support

Primary sponsor: Editas Medicine, Inc.
Source(s) of monetary or material Support: Farmaceutisch Bedrijf;Editas Medicine;Inc. ;Allergan Inc

Intervention

Keyword: CEP290, Natural History, Retinal Degeneration

Outcome measures

Primary outcome

The feasibility, test/retest variability, and changes over time of key

assessments in participants with CEP290-related retinal degeneration.

Whether the Visual Function Navigation Test as a clinically meaningful endpoint

of functional vision in participants with CEP290-related retinal degeneration.

Secondary outcome

CEP290-related retinal degeneration and the clinical phenotype of participants

with light perception to 20/50 visual acuity and with either compound

heterozygous or homozygous intron 26 c.2991+1655A>G mutations

Study description

Background summary

A deficiency in CEP290 protein in photoreceptors leads to defects in the connecting cilium and
outer segments of photoreceptor cells (Parfitt, 2016), thereby causing photoreceptor dysfunction,
retinal degeneration, and blindness (Yildiz, 2012). In patients with LCA10, there is a striking
disconnect between the structure and function of the fovea, such that even patients with little or no
vision retain a central island of photoreceptors in the fovea (cones) and surrounding macula (cones
and rods) (Cideciyan, 2007; Boye, 2014). These and other factors suggest that there is a window of opportunity to intervene in the
disease process to restore vision. The Sponsor is planning to conduct a prospective natural history study with systematic
assessments and uniform follow-up that will provide a high-quality dataset for assisting in the

design of future clinical treatment trials involving patients with CEP290-related retinal
degeneration caused by the common intron 26 mutation.

Study objective

The primary objectives of this study are the following:
* To prospectively characterize CEP290-related retinal degeneration and the clinical phenotype
of participants with light perception to 20/50 visual acuity and with either compound heterozygous or homozygous intron 26 c.2991+1655A>G mutations;
* To evaluate the feasibility, test/retest variability, and changes over time of key assessments in
participants with CEP290-related retinal degeneration; and
* To gather information to support validation of the Visual Function Navigation Test as a clinically meaningful
endpoint of functional vision in participants with CEP290 related retinal degeneration.

Study design

This is an international, multicenter study to assess the natural history of CEP290-related retinal degeneration caused by a compound heterozygous or homozygous intron 26 c.2991+1655A>G mutation.No randomization will be performed. Every attempt will be made to recruit 5 participants in each of 8 cohorts (6 in the Netherlands), comprising 4 age ranges (3 in the Netherlands) and 2 visual acuity ranges. At the beginning of the study, Principal Investigators are requested to provide the number of potential participants based on age group and visual acuity to get a better idea of the number of participants per cohort. Cohorts will be enrolled in parallel. The purpose of the different cohorts is to ensure a broad spectrum of participants for the natural history analyses and for validating the Visual Function Navigation Test. If it is not possible to enroll the targeted number of five participants per cohort, additional participants may be enrolled in the other cohorts to maintain the overall sample size at 40 participants. Study visits will occur at Screening, Baseline (test and retest), and Months 3, 6, and 12 for a total study duration of approximately 1 year. Study endpoint will be at 1 year. Both eyes of each participants will be evaluated during the course of this natural history study. All analyses will be based on all enrolled particpants overall and also by cohort.

Study burden and risks

Risks: Risks associated with the study procedures: blood draw, opthalmic assessments

Burden: the invested time and filling in questionnaires about quality of life can be experienced as burden

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)

Inclusion criteria

1. pariticipants and/or parent/legal guardian must complete/sign an informed consent form (ICF). If
required on a per participants basis, provisions can be made for alternative forms of consent
(eg, witnessed consent). Where required by the IRB/IEC, minors must also verbalize or sign a

confirmation of assent. Refer to Section 11.3;
2. Male or female participants >=6 years of age at Screening;
3. Has abnormally decreased vision, defined as having light perception to 20/50 best-corrected visual acuity (BCVA) in
each eye, with examination and test results consistent with an inherited retinal degeneration
due to mutations in the CEP290 gene;
4. Has CEP290-related retinal degeneration caused by a compound heterozygous or homozygous
intron 26 c.2991+1655A>G mutation (ie, 1 or 2 copies of the intron 26 c.2991+1655A>G
mutation) confirmed by deoxyribonucleic acid sequencing;
5. Has ability to cooperate with assessments relative to age;
6. Has clear ocular media and adequate pupil dilation in at least 1 eye, to permit good quality
fundus examination and optical coherence tomography (OCT) imaging; and
7. For females of childbearing potential: is not pregnant as confirmed by a negative urine pregnancy test at Screening and is not planning to become pregnant during the course of the study.

Exclusion criteria

1. Has history or current evidence of a medical condition (systemic or ophthalmic disease,
metabolic dysfunction, physical examination finding, or clinical laboratory finding) that may,
in the opinion of the Investigator, preclude adherence to the scheduled study visits, safe
participation in the study, or affect the results of the study (eg, uncontrolled systemic
hypertension, autoimmune disease, advanced coronary artery disease, or cerebral vascular
disease, other unstable or progressive cardiovascular, pulmonary, Parkinson's, liver or renal
disease, cancer, or dementia);
2. Has history or current evidence of ocular disease in either eye that, in the opinion of the
Investigator, may confound assessment of this inherited retinal disease or the assessments
utilized herein (eg, glaucoma, age-related macular degeneration, diabetic retinopathy, uveitis,
or the presence of any condition that precludes adequate visualization of the fundus such as
dense cataracts or corneal scarring);
3. Achieves a passing score for the Visual Function Navigation Test at the

maximum level of difficulty (ie. passes the most challenging Visual Function Navigation Test under the dimmest lighting conditions) with each eye independently and both eyes together;
4. Is currently receiving gene therapy and/or has received gene therapy or oligonucleotide therapeutics;
5. Is currently enrolled in an investigational or interventional drug or device study and/or has
participated in such a study within 30 days of Screening.
6. For females of childbearing potential: is pregnant (or planning to become pregnant) or breastfeeding.

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	11-01-2019
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO Date:	23-08-2018
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-11-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO Date:	19-11-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	15-06-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	08-07-2021
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
CCMO	NL64968.091.18

Study results

Date completed:	10-03-2022
Results posted:	25-04-2023
Actual enrolment:	4

First publication
28-03-2023