Prospective clinical evaluation of Stargardt disease patients with the appropriate genotype for development of antisense oligonucleotide therapy

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Ocular structural change, deposit and degeneration NEC
Study type	Observational non invasive

Summary

ID

NL-OMON51692

Source
ToetsingOnline

Brief title
STGD1 for AON

Condition

- Ocular structural change, deposit and degeneration NEC

Synonym
Inherited retinal disease, Stargardt disease

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum

Source(s) of monetary or material Support: Foundation Fighting Blindness USA

Intervention

Keyword: ABCA4, Inherited retinal diseases, Natural history, Stargardt disease

Outcome measures

Primary outcome

Best corrected visual acuity, atrophic lesion size measured by fundus autofluorescence, mean retinal sensitivity as measured by fundus-guided microperimetry, area of ellipsoid zone loss as measured by SD-OCT, visual field sensitivity measured by static perimetry, macular and retinal function using multifocal and full-field ERG amplitudes and implicit time, rod and cone full-field stimulus thresholds.

Secondary outcome

patient reported outcomes (questionnaire)

Study description

Background summary

Currently, there is no effective therapy for Stargardt disease (STGD1). STGD1 is caused by mutations in the ABCA4 gene. Several of these mutations are amendable to antisense oligonucleaotide-based (AON) therapy. AONs have shown promising results in clinical trials for other subtypes of retinal disease and appear to be a good candidate therapeutic for STGD1. The current study aims to define the natural history and clinical outcome parameters in STD1 patients with the appropriate genotype for AON therapy. This will result in a better understanding of the baseline progression of the disease and identification of the best clinical outcomes to measure therapeutic efficacy in clinical trials with AONs following completion of this project.

Study objective

The goal of this study is to characterize the natural history of STGD1 patients

with the appropriate genotype for AON therapy and to identify the best clinical outcomes to measure therapeutic efficacy in clinical trials following completion of this study.

Study design

Longitudinal observational cohort study.

Study burden and risks

Participants do not benefit, risks are considered negligible, procedures are non-invasive and take 3 to 7 hours per visit, 2 visits per year for a total of 2 years. It is anticipated that, in the future, STGD1 patients will benefit from AON therapy.

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)
Elderly (65 years and older)

Inclusion criteria

Study Participant Inclusion Criteria
In order to be eligible to participate in this study, a subject must meet all of the following criteria:
1. Clinical diagnosis of STGD1 and at least one pathogenic or likely pathogenic mutation and one of the mutations should be either c.768G>T, c.4539+2001G>A or c.5196+1137G>A
2. Willingness and ability to participate in this study and to complete the informed consent
3. Willingness and ability to return for the five study visits over 24 months
4. Age >= 6 years

Ocular Inclusion criteria
Both eyes of the participant must meet the following criteria:
1. Baseline visual acuity ETDRS letter score of 35 or more (approximate Snellen equivalent 20/200 or better, decimal acuity >=0.1)
2. Stable fixation and ability to perform perimetry reliable
3. Clear ocular media and adequate pupil dilation to permit good quality imaging

Exclusion criteria

If either of one eyes has any of the following, the patient is not eligible to participate in this study:
1. Current vitreous haemorrhage
2. Current or any history of tractional or rhegmatogenous retinal detachment
3. Current or any history of (e.g., prior to cataract or refractive surgery) spherical equivalent of the refractive error worse than -8 diopters of myopia
4. History of intraocular surgery (e.g., cataract surgery, vitrectomy, penetrating keratoplasty, or LASIK) within the last 3 months
5. Current or any history of retinal vascular occlusion of proliferative diabetic retinopathy
6. Expected to have cataract removal during the study
7. History of current evidence of ocular disease that, in the opinion of the investigator, may confound assessment of visual function
8. Current participation in a clinical trial for treatment of STGD1
9. History of participation in a clinical trial for treatment of IRD with irreversible effect, like gene-therapy
10. History of participation in a clinical trial for treatment of STGD1 with

reversible effect, for which the wash-out time has not yet passed

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	24-08-2022
Enrollment:	60
Type:	Actual

Ethics review

Approved WMO

Date:	13-04-2022
Application type:	First submission
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	NL80174.091.21