Prospective clinical trial to evaluate the efficacy of acetazolamide for the treatment of cystoid macular edema in inherited retinal dystrophies: the CAR trial

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Our study objective is to evaluate the efficacy of acetazolamide for the treatment of cystoid macula edema in inherited retinal dystrophies in anticipation of future clinical trials.

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

Summary

ID

NL-OMON51635

Source
ToetsingOnline

Brief title
The CAR trial

Condition

- Retina, choroid and vitreous haemorrhages and vascular disorders

Synonym
Inherited retinal dystrophies, Inhertited retinal diseases

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Acetazolamide, Cystoid Macular Edema, Inherited retinal dystrophies

Outcome measures

Primary outcome

The main endpoint is the to determine the effective dosage, the outcome of the treatment, and the effect on the visual acuity. As such, these findings will have immediate impact on translational scientific progress, by applying cutting-edge multidisciplinary technology to facilitate patient identification and selection for novel treatments.

Secondary outcome

Secondary study endpoints include the following compared within the treated group and compared to control group:

1) To determine the optimal acetazolamide dose for maximum effect on CME and minimal side effects

2) To determine the intra- and inter individual variability in such treatment- and side effects

3) To determine the proportion of IRD patients with CME in which acetazolamide treatment is able to completely resolve CME for a spectrum of different IRD-associated genes

Study description

Background summary

Inherited retinal dystrophies (IRDs) encompass a spectrum of severe eye diseases, characterized by progressive loss of retinal structure and visual function. Besides marked vision loss, IRDs may be complicated by cystoid macular edema (CME) in the macula (the center of the retina, responsible for detailed vision, color and contrast vision). The presence of CME has been reported to have a possible negative effect on central vision and disease progression. Moreover, IRD patients with CME may not be eligible for upcoming innovative treatments such as gene therapy. Therefore, it is of the utmost importance to try to effectively treat CME with existing potential treatment options, not only to reduce the risk of vision loss, but also to increase chances for patients to be eligible for future (gene) therapy.

Study objective

Our study objective is to evaluate the efficacy of acetazolamide for the treatment of cystoid macula edema in inherited retinal dystrophies in anticipation of future clinical trials.

Study design

Investigator-initiated, single-center, prospective, experimental study consisting of seven visits at 2, 4, 8, 12, 16, and 32 weeks after baseline evaluation visit. During each visit participants will perform several ophthalmological measurements

Intervention

The used intervention in this study is acetazolamide, which belongs to a class of drugs known as carbonic anhydrase inhibitors and has been used with other medications to treat high pressure inside the eye due to certain types of glaucoma.

Study burden and risks

Acetazolamide will be used during this study and there is possible risk of uncommon (infrequent) to very rare adverse events as mentioned in the Summary of Product Characteristics. Also, participants (especially young children and elderly) may experience a minimal physical burden of visiting the hospital seven times in 32 weeks. Additionally, patients may feel confronted with their visual impairments.

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)
Elderly (65 years and older)

Inclusion criteria

Eligible patients received a clinical diagnosis of IRD, and underwent at least one clinical examination, in combination with one of the following prerequisites:
• IRD associated with causal genetic variant(s) (in e.g., USH2A, CRB1, RHO, RP1, RP2, RPGR, PRPF31, or RS1 gene)
• CME involving the fovea confirmed on spectral-domain optical coherence tomography (OCT)

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
• Eyes will be excluded when the visual dysfunction is also significantly associated with other ocular diseases besides the IRDs (e.g., glaucoma, perforating trauma).
• Patients treated with loop diuretics
• Severe hepatic impairment
• Severe renal insufficiency
• Sodium and Potassium Depletion
• Addison's disease
• Hyperchloremic Acidosis
• Cor pulmonale
• Chronic non-congestive angle-closure glaucoma
• The use of Acetazolamide
• • Patients treated with interacting medication such as:
o Folic acid antagonists: methotrexate, trimethoprim and pyrimethamine
o Hypoglycaemics
o Oral anti-coagulants
o Asprin
o Cardiac glycosides: digoxine
o diuretics, such as thiazides and loop diuretics:
o anticonvulsants such as: phenytoin, primidone and carbamazepine
o Carbonic Anhydrase Inhibitors
o Procaine
o Sodium hydrogen carbonate
o Cyclosporine
o Ephedrine, methadone, amphetamine, quinidine and lithium

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	20-01-2023
Enrollment:	18
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Acetazolamide
Generic name:	DIAMOX
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	31-05-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-09-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-12-2022
Application type:	First submission
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	EUCTR2002-000237-17-NL
CCMO	NL80249.018.22