Study on half-dose Photodynamic therapy versus Eplerenone in chronic CenTRAl serous chorioretinopathy (SPECTRA trial)

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Primary Objective: to investigate whether half-dose PDT treatment leads to a higher percentage of cCSC patients with SRF on OCT at baseline, achieving an absence of this SRF on OCT as compared to eplerenone treatment.Secondary Objectives: to...

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

Summary

ID

NL-OMON50407

Source
ToetsingOnline

Brief title
SPECTRA trial

Condition

- Retina, choroid and vitreous haemorrhages and vascular disorders

Synonym
chronic central serous chorioretinopathy

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum

Source(s) of monetary or material Support: fondsen

Intervention

Keyword: chronic central serous chorioretinopathy, eplerenone, half-dose photodynamic therapy, treatment

Outcome measures

Primary outcome

The primary endpoint of this study is to assess if there is a difference between half-dose PDT and eplerenone treatment in patients with cCSC, in terms of complete resolution of SRF on OCT. The assessment of this efficacy will be based on the anatomical effect on OCT: absence of SRF versus persistence of SRF, at 3 months after the initiation of treatment.

Secondary outcome

As secondary endpoints, we will mainly look at 3 parameters that reflect the patient*s vision-related functioning. These 3 parameters are: a standardized measurement of ETDRS BCVA, a standardized measurement of sensitivity of the macula with microperimetry, and a standardized assessment of the patient*s vision-related quality of life using a validated questionnaire, the NEI-VFQ-25.

The secondary endpoints that will be assessed as a reflection of functional improvement after treatment include:

- Number of cross-over treatments (eplerenone after half-dose PDT, and half-dose PDT after eplerenone) needed in each treatment arm;
- Mean change in ETDRS BCVA in the study eye at Evaluation Visit 1, at - if applicable - Evaluation Visit 2, at Evaluation Visit 3, and at the Final

Evaluation Visit, compared to Baseline Evaluation;

- Mean change in ETDRS BCVA in the study eye at Evaluation Visit 3 and at Final Evaluation Visit among those with subsequent (cross-over) and those without subsequent treatment;

- Mean change in retinal sensitivity in the study eye at Evaluation Visit 1, at - if applicable - Evaluation Visit 2, at Evaluation Visit 3, and at Final Evaluation Visit, compared to Baseline Evaluation;

- Mean change in the NEI-VFQ-25 questionnaire at Evaluation Visit 1, at - if applicable - Evaluation Visit 2, at Evaluation Visit 3, and at Final Evaluation Visit, compared to Baseline Evaluation;

- The long-term outcome both after successful treatment and after non-successful treatment (*success* is defined as the absence of SRF on OCT at Evaluation Visit 1 (at 3 months after the initiation of treatment));

- Differences between starting with treatment A with the possibility to switch to treatment B compared to starting with treatment B with the possibility to switch to treatment A;

- The number of (S)AEs in the 2 different treatment groups.

Study description

Background summary

The proposed study is the first prospective randomized controlled trial that compares half-dose PDT with eplerenone treatment in patients with chronic central serous chorioretinopathy, with regard to their ability to achieve complete resolution of SRF, and their ability to improve the quality of vision. In this study, we have chosen half-dose PDT since it is considered to be the standard treatment for cCSC in many centers worldwide. Eplerenone treatment has

been chosen as the treatment of choice in the control arm, because this relatively new and non-invasive therapy for cCSC has been described to lead to promising results, and to less AEs in comparison with the other mineralocorticoid antagonist spironolactone. Eplerenone treatment for cCSC is also used as standard first-line treatment in many centers worldwide. A multicenter randomized controlled trial, in which half-dose PDT and high-density micropulse laser treatment are included, is currently conducted and led by our group.
In this study, we want to define treatment success not only on the basis of structural parameters (absence of SRF on optical coherence tomography (OCT) after treatment), but also based on functional vision-related endpoints, both on the short-term and long-term. With the results of this study we hope to establish a strong scientific foundation for further research on the optimal treatment of patients with cCSC to improve the visual outcome and quality of life of this relatively frequently occurring retinal disease.

Study objective

Primary Objective: to investigate whether half-dose PDT treatment leads to a higher percentage of cCSC patients with SRF on OCT at baseline, achieving an absence of this SRF on OCT as compared to eplerenone treatment.
Secondary Objectives: to investigate the clinical outcome comparing half-dose PDT treatment with eplerenone treatment in patients with SRF due to active leakage in cCSC, based on evaluation of best-corrected visual acuity, retinal sensitivity on microperimetry, and subjective scores on the National Eye Institute Visual Function Questionnaire.

Study design

This study is a multicenter, prospective, randomized, and controlled, open-label study that will compare the efficacy and safety of 2 treatments in patients with cCSC. The first group of patients will receive half-dose PDT treatment. The second group of patients will receive eplerenone treatment. Each patient will receive at least 1 treatment, but may be eligible to receive a cross-over treatment after the evaluation visit at 3 months after the initiation of treatment, from either half-dose PDT to eplerenone, or from eplerenone to half-dose PDT. Potentially eligible patients will be identified from 3 ophthalmology trial sites in the Netherlands.
Multimodal imaging (fundus photographs, FA, ICGA, and OCT images) collected at the Baseline Evaluation will be sent to a central reading center (CRC). The CRC will review these images to confirm subject eligibility based on the characteristics specified in the inclusion criteria. Once eligibility has been confirmed by the CRC, all other inclusion and exclusion criteria have been met at the Baseline Evaluation, and informed consent (IC) has been obtained, patients will be enrolled in the trial.
There are 9 examinations that will be performed at the Baseline Evaluation, 3

months after the initiation of treatment (at Evaluation Visit 1), and 3 months after the possible initiation of cross-over treatment (Evaluation Visit 2). The necessity of the performance of FA and ICGA at Evaluation Visit 3 and at Final Evaluation Visit will be according to the discretion of the treating ophthalmologist. In principle, FA and ICGA images will be acquired when there is persistent SRF on OCT at Evaluation Visit 3 and Final Evaluation Visit.
The 6 anatomical assessments include ophthalmoscopy, fundus photography, OCT (including OCT angiography), autofluorescence imaging, FA, and ICGA. The 3 functional assessments include visual acuity measurement, microperimetry, and a questionnaire on vision-related functioning.
Enrolled patients will be randomized at a 1:1 ratio to receive half-dose PDT treatment or eplerenone treatment. When contra-indications for the prescription of eplerenone will be detected after Baseline Evaluation, these patients will receive half-dose PDT.

The total number of visits per patient for this trial is 5 (in case of 1 required treatment) or 7 (in case of 2 required treatments). The duration of participant participation from the beginning until the end of study is 24 months.

Intervention

In the half-dose PDT treatment arm, all patients will receive an intravenous drip through which half-dose (3 mg/m2) verteporfin (Visudyne ®) is administered, with an infusion time of 10 minutes. At 15 minutes after the start of the infusion, PDT laser treatment is performed with standard 50 J/cm2 fluency, PDT laser wavelength of 689 nm, and treatment duration of 83 seconds. For treatment with PDT in cCSC patients, the administration of verteporfin has previously been considered not to be study medication.
In the eplerenone arm, patients will receive 25 mg eplerenone once daily for 1 week, and when no abnormalities will be detected in the serum potassium, 50 mg eplerenone will be taken orally once daily until 3 months after initiation of treatment.

Study burden and risks

The included patients in this study do not have to attend additional visits, and no additional invasive procedures will be performed within this study. The only additional procedure to be carried out by the included patients is the answering of questionnaires.
Both treatments are currently prescribed to cCSC patients worldwide. One of the possible outcomes of this randomized controlled trial is that a treatment could be superior to the other, but a cross-over of treatment will be performed when complete resolution of SRF does not occur at 3 months after the initiation of treatment (Evaluation Visit 1).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

This study will enroll subjects with chronic central serous chorioretinopathy (cCSC) with active leakage of fluid to under the retina as evidenced on optical coherence tomography (OCT) scanning and further supported by findings on fluorescein angiography (FA) and indocyanine green angiography (ICGA), in at least 1 eye, who visit the outpatient clinic of the Department of Ophthalmology of the Radboud University Medical Center, the Academic Medical Center Amsterdam, or the Leiden University Medical Center. If both eyes are eligible, then the eye with the longer duration of disease will be used as the study eye, except in cases where the disease is present for more then 18 months. In the latter case, which is an exclusion criterion, the other eye will be eligible for inclusion if the disease is active for less then 18 months in that eye. If the non-study eye also has active disease, the choice to treat and the type of

treatment in this eye may be chosen freely at the discretion of the responsible ophthalmologist.
Before enrolment, each subject must meet all of the following inclusion criteria and none of the exclusion criteria, and agree to comply with the study requirements including completion of all of the study visits.In order to be eligible to participate in this study, a subject must meet all of the following criteria:
- Age of >= 18 years of age and able to give written informed consent;
- Active cCSC;
- Subjective visual loss for more then 6 weeks, interpreted as onset of active disease;
- Foveal subretina fluid on OCT, at Baseline Examination;
- >=1 ill-defined hyperfluorescent leakage areas on FA with retinal pigment epithelial window defect(s) that are compatible with cCSC;
- Hyperfluorescent areas on ICGA.Bá*CBC

Exclusion criteria

A potential subject who meets any of the following criteria for the study eye will be excluded from participation in this study:
- Any previous treatments for active CSC;
- Previous prescription of mineralocorticoid receptor antagonists, for cCSC or for other diseases;
- Current treatment with corticosteroids (topical or systemic), corticosteroid use within 3 months before possible start of trial treatment, or anticipated start of corticosteroid treatment within the first 2 years from the start of the trial period;
- Evidence of another diagnosis that can explain serous SRF or visual loss;
- BCVA < 20/200 (Snellen equivalent);
- Profound chorioretinal atrophy in central macular area on ophthalmoscopy and OCT;
- Myopia > 6D;
- Visual loss and/or serous detachment on OCT < 6 weeks;
- Continuous and/or progressive visual loss > 18 months or serous detachment on OCT > 18 months;
- No hyperfluorescence on ICGA;
- Intraretinal edema on OCT;
- (relative) Contraindications for FA or ICGA;
- (relative) Contraindications for PDT treatment (pregnancy, porphyria, severely disturbed liver function). Pregnancy will not be routinely tested in female patients, but the possibility of pregnancy will be discussed during screening;
- (relative) Known contraindications for initiation of eplerenone treatment (hyperkalemia, abnormal renal clearance, severe hepatic insufficiency (Child-Pugh C), type 2 diabetes mellitus with microalbuminuria, concomitant use

of potassium supplements, potassium-sparing diuretics, strong CYP3A4 inhibitors, or the combination of an ACE-inhibitor and an angiotensin receptor blocking agent). Pregnancy will not be routinely tested in female patients, but the possibility of pregnancy will be discussed during screening;
- Soft drusen in treated eye or fellow eye, signs of choroidal neovascularization on ophthalmoscopy and/or FA/ICGA of the study eye. The previous prescription of oral medication (for example, acetazolamide) for cCSC, except the prescription of previous mineralocorticoid receptor antagonists, is not an exclusion criterion for this study.BKKá*J

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-02-2017
Enrollment:	107
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Inspra
Generic name:	eplerenone
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	09-11-2016
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	19-12-2016
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	12-04-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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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
Other	2016-004119-11

Register	ID
EudraCT	EUCTR2016-004119-11-NL
CCMO	NL59158.058.16