A 12-month, phase IV, randomized, open label, multicenter study to compare efficacy of 0.5 mg ranibizumab PRN versus 2 mg aflibercept bimonthly intravitreal injections on retinal thickness stability till month 6 of treatment and explore functional outcomes up to month 12 in patients with neovascular (wet) age-related macular degeneration (AMD) (CRFB002ADE23, SALT study)

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Primary: to compare the treatment effect of ranibizumab PRN (visual acuity loss and/or SD-OCT disease activity guided retreatment) versus aflibercept bimonthly regimen on central retinal thickness stability as measured by mean fluctuations between...

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

Summary

ID

NL-OMON44213

Source
ToetsingOnline

Brief title
CRFB002ADE23, SALT

Condition

- Retina, choroid and vitreous haemorrhages and vascular disorders

Synonym
wet macular degeneration

Research involving
Human

Sponsors and support

Primary sponsor: Novartis
Source(s) of monetary or material Support: Novartis Pharma BV

Intervention

Keyword: aflibercept, AMD, ranibizumab

Outcome measures

Primary outcome

Central retinal thickness up to month 6.

Secondary outcome

Visual acuity, retinal stress. Adverse events.

Study description

Background summary

Age-related macular degeneration (AMD) is the leading cause of severe loss of vision in the elderly population. The depositions between the retinal epithelium and Bruch*s membrane, known as drusen, is a main predictor of a progressive and degenerative process, in which an advanced AMD, neovascularization and atrophy, can be the final result.
In recent years earlier diagnosis, close monitoring (e.g. OCT) and efficacious and safe medications (such as ranibizumab) of patients with neovascular (wet) AMD (wAMD) have contributed to a decrease of cases of blindness as well as improve the quality of life of the patients with this degenerative disease.
The current ranibizumab label in the EU recommends the monitoring of VA and the

interruption and re-initiation of treatment primarily based on VA assessments. When stable VA (based on 3 consecutive monthly observations) is observed, treatment can be interrupted. If, again, a loss of VA is observed, treatment is re-initiated.
Since the approval of Lucentis (ranibizumab) there have been several clinical studies that have evaluated a PRN (*if needed*) treatment algorithm including guidance by OCT, but the results have been variable.
Despite the fact that OCT imaging is commonly used in clinical practice, there is limited randomized clinical trial evidence on the use of OCT guided treatment algorithms. Since OCT findings may play a key role in the treatment decisions, there is need to generate additional data from large clinical studies. Advances in OCT technology have led to the development and more widespread use of spectral domain OCT (SD-OCT), and this study will use SD-OCT to measure central retinal thickness.
This study will evaluate and compare the efficacy and safety of two approved wAMD treatment drugs with their associated distinct regimens aiming to achieve and maintain stable central subfield retinal thickness and prevent retinal stress. Ranibizumab will be administered PRN with a best-corrected visual acuity (BCVA) loss and/or OCT disease activity guided retreatment and aflibercept according to its approved European label (continuous treatment for the first year).

Study objective

Primary: to compare the treatment effect of ranibizumab PRN (visual acuity loss and/or SD-OCT disease activity guided retreatment) versus aflibercept bimonthly regimen on central retinal thickness stability as measured by mean fluctuations between Month 3 and 6.
Secondary: to demonstrate correlation of functional outcome (visual acuity) at month 12 with retinal stress, defined as significant fluctuations in central retinal thickness, parameters as measured by SD-OCT up to month 6. Safety.

Study design

Multicenter randomized open-label phase IV parallel-group study.
Randomization (1:1) to one of the treatment regimens:
* 0.5 mg intravitreal injections of ranibizumab monthly until maximum stable BCVA with retreatment based on BCVA loss and/or SD-OCT disease activity.
* 2 mg intravitreal injections of aflibercept monthly for the first 3 months, followed by 2 mg intravitreal injections once every 2 months (current EU SmPC label).
Treatment of one eye. If both eyes are affected: the *study eye* will be chosen by the investigator. The treatment of the other eye will be selected by the investigator.
Study duration 12 months.
Approx. 706 patients.

Intervention

Treatment with ranibizumab or aflibercept.

Study burden and risks

Risk: Adverse effects of study medication.
Burden: Study duration approx. 12 months. Screening, baseline, thereafter monthly visits and end of study visit. Duration mostly 2-6 h.
Ranibizumab: monthly intravitreal injections (at least 3) until stable BCVA.
Retreatment with monthly injections based on BCVA plus/minus OCT paramaters.
Aflibercept: monthly injections during first 3 months, thereafter every 2 months.
Monthly ophthalmic examinations, incl. OCT.
Angiography at screening, months 3, 12.
At screening 4 ml blood in women of childbearing potential for pregnancy test
Questionnaire quality of life, at screening, months 3, 12.
In selected centres: electroretinography and assessment of contrast sensitivity.
Optional: biomarker research (3-8 times 20 ml blood and 2 extra visits for a blood draw).

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

* Male or female patients 18 years and above.
* Visual impairment predominantly due to neovascular AMD.
* Active, newly diagnosed, untreated, angiographically documented CNV lesion (see protocol page 21 for details) secondary to AMD.

Exclusion criteria

* Pregnant or lactating women. Women of child-bearing potential, not practicing adequate contraception.
* Stroke or myocardial infarction less than 3 months prior to screening.
* Systolic BP >160 mm Hg or diastolic BP >100 mm Hg at Screening or Baseline.
* Any active (peri)ocular infection or inflammation.
* Uncontrolled glaucoma (intraocular pressure*30 mm Hg on medication).
* Neovascularization of the iris or neovascular glaucoma.
* Exclusion criteria study eye and prior or current medications: see protocol page 22-23.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-11-2014
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Eylea
Generic name:	aflibercept
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Lucentis
Generic name:	ranibizumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	11-03-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-06-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-11-2014
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-12-2014
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-07-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-07-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-10-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-10-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-02-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-02-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	clinical trials.gov; NCT01958918
EudraCT	EUCTR2013-002431-15-NL
CCMO	NL48042.018.14