# A PHASE III, MULTICENTER, RANDOMIZED, DOUBLE-MASKED, SHAM-CONTROLLED STUDY TO ASSESS THE EFFICACY AND SAFETY OF LAMPALIZUMAB ADMINISTERED INTRAVITREALLY TO PATIENTS WITH GEOGRAPHIC ATROPHY SECONDARY TO AGE-RELATED MACULAR DEGENERATION

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EFFICACY OBJECTIVESThe primary efficacy objective of this study is to evaluate the efficacy of intravitreal injections of 10 mg lampalizumab administered Q4W or Q6W in CFI profile biomarker positive and CFI profile biomarker-negative patients...

| | |
|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Vision disorders |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON41475

**Source**
ToetsingOnline

**Brief title**
GX29185 - SPECTRI

### Condition

- Vision disorders

**Synonym**
Geographic Atrophy secondary to age related macular degeneration

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Roche Nederland B.V.
**Source(s) of monetary or material Support:** F. Hoffmann La Roche Ltd.

## Intervention

**Keyword:** double masked, Lampalizumab, Macular Degeneration, Phase III

## Outcome measures

### Primary outcome

The primary efficacy outcome measure for this study is GA area at 1 year as

assessed by FAF.

### Secondary outcome

The secondary efficacy outcome measures for this study over time are as follows:

• Number of scotomatous points assessed by mesopic microperimetry for the

evaluation of the macular functional response

• Change in macular sensitivity as assessed by mesopic microperimetry for the

evaluation of the macular functional response

• GA area as assessed by FAF

• BCVA score as assessed by ETDRS chart at a starting distance of 4 m

• BCVA score as assessed by ETDRS chart under low luminance conditions at a

starting distance of 4 m

• Binocular reading speed as assessed by MNRead charts or Radner Reading Charts

• Binocular critical print size as assessed by MNRead charts or Radner Reading

Charts

• NEI VFQ-25 composite score

• NEI VFQ-25 near activity subscale score

• NEI VFQ-25 distance activity subscale score

• FRI Index score

For further information see page 39-40 of the protocol

# Study description

**Background summary**

Age-related macular degeneration (AMD) is the leading cause of irreversible blindness in people aged 50 years or older in the developed world. The majority of the visual loss occurs in the advanced stage of AMD, which has two clinical forms: a non-exudative form, geographic atrophy (GA), which is characterized by loss of choriocapillaris, retinal pigment epithelium (RPE), and photoreceptors; and an exudative or wet form, which is characterized by choroidal neovascularization (CNV). The prevalence of GA increases exponentially with age and approximately quadruples per decade beyond 50 years of age. The estimated prevalence of GA in populations of European ancestry at 70 years of age is 0.70%, rising to 2.91% at 80 years of age and 11.29% at 90 years of age.

Currently, there are no approved treatments to prevent the worsening of GA or the associated declines in visual function. Consequently, a significant unmet need exists for the treatment of this serious condition. The Phase III clinical development plan for lampalizumab is designed to test the efficacy and safety of lampalizumab in patients with GA secondary to AMD.

**Study objective**

EFFICACY OBJECTIVES
The primary efficacy objective of this study is to evaluate the efficacy of intravitreal injections of 10 mg lampalizumab administered Q4W or Q6W in CFI profile biomarker positive and CFI profile biomarker-negative patients compared with sham control assessed by change in the GA area from baseline as measured by FAF.

The secondary efficacy objective of this study is to evaluate the effect of lampalizumab compared with sham control, with respect to:
• Macular functional response as assessed by mesopic microperimetry
• Best corrected visual acuity (BCVA) as measured by the Early Treatment Diabetic Retinopathy Study (ETDRS) chart (at a starting distance of 4 m)
• BCVA as measured by ETDRS chart (at a starting distance of 4 m) under low luminance conditions
• Binocular reading speed as assessed by the Minnesota Low-Vision Reading Test (MNRead) or by Radner Reading Charts
• Binocular critical print size as assessed by the MNRead or by Radner Reading Charts
• Patient-reported visual function as assessed by the National Eye Institute Visual Functioning Questionnaire 25-item Version (NEI VFQ-25)
• Patient-reported independent reading as assessed by the Functional Reading Independence Index (FRI Index)

SAFETY OBJECTIVES
The safety objectives for this study are as follows:
• To evaluate the local and systemic safety and tolerability of intravitreal injections of 10-mg lampalizumab administered Q4W or Q6W relative to sham control
• To evaluate the clinical significance of anti-therapeutic antibodies directed against lampalizumab
PHARMACOKINETIC OBJECTIVE
The PK objective for this study is to characterize the systemic PK of lampalizumab administered by 10-mg intravitreal injections Q4W or Q6W.
DIAGNOSTIC OBJECTIVE
A diagnostic objective for this study is to evaluate the prognostic value of the CFI profile biomarker on the mean change in the GA area from baseline as measured by FAF.
EXPLORATORY OBJECTIVES
The exploratory objectives for this study are as follows:
• To evaluate the effect of lampalizumab compared with sham control, with respect to:
- Monocular reading speed as assessed by MNRead charts or by Radner Reading Charts
- Monocular critical print size as assessed by MNRead charts or by Radner Reading Charts
- Monocular reading acuity as assessed by MNRead charts or by Radner Reading Charts
- Binocular reading acuity as assessed by MNRead charts or by Radner Reading Charts
• To evaluate the aqueous levels of total lampalizumab and factor D following intravitreal injection
• To evaluate the potential association of genetic variants in CFI and complement pathway genes with disease characteristics and response to administration of lampalizumab

• To evaluate the relationship of genetic variants in CFI and complement-pathway genes to levels in the blood of messenger RNA (mRNA) and proteins of CFI and complement-pathway genes

## Study design

This study is a Phase III, double-masked, multicenter, randomized, sham injection controlled study evaluating the efficacy and safety of a 10-mg dose of lampalizumab administered Q4W or Q6W by intravitreal injections for approximately 96 weeks, excluding screening period, in patients with GA secondary to AMD.

## Intervention

Patients that participate in the study will be treated with lampaluzimab or a sham injection in a Q4Q or Q6W dosing schedule

## Study burden and risks

The patient can experience side effects from the medicine or procedures that are used in this study. The side effects can vary from light to very serious and will differ from person to person. Everyone that participates in this study is closely monitored on possible side effects. The sponsor, investigator and other physicians do not know all side effects that might occur. The investigator can prescribe the patient medication to help decrease the side effects. A lot of side effects disappear when the cause of the side effects is taken away. In some cases side effects may be severe, persist or never disappear. There is a risk of death. In a recently completed study patients with GA received an injection every month or every other month. The experience retrieved in that study show that administration of injections with lapalizumab where well tolerated over time.

SIDE EFFECTS FROM WHICH IS KNOWN TO BE RELATED TO INJECTION OF THE STUDY MEDICATION (LAMPATIZUMAB) AND OR INJECTION IN THE EYE
There are events that have been reported by a small number of patients after the use of lampalizumab in previous clinical trials. These events, which have been seen with other injections into the eye, have also been seen with use of lampalizumab. The frequencies listed below are based on use of lampalizumab in a total of 147 patients, who were enrolled in prior clinical trials.
Very Common (Occur in at least 1 in 10 patients treated):
• Bleeding of the thin membrane covering the white of the eye and inner lid,
• Temporary increase in the pressure in the eye, and
• Eye pain
Common (Occur in at least 1 in 100 to 1 in 10 patients treated):
• Eye irritation,
• Swelling of the thin membrane covering the white of the eye and inner lid,

• Feeling that there is something in the eye,
Uncommon (Occur in at least 1 in 1000 to 1 in 100 patients treated):
• A serious eye infection called endophthalmitis

SIDE EFFECTS THAT ARE POSSIBLY RELATED WITH INJECTIONS OF THE STUDY MEDICATION (LAMPALUZIMAB) AND/OR INJECTION IN THE EYE COMPLICATIONS RELATED TO THE EYE
There is a change that your eyesight worsens; this can be caused due to worsening of your eye disease, due to a side effect of the injection with the study treatment or other causes. The study medication can cause infections in the eye that cans how as redness, swelling or pain in the eye. This infection does not have to be related with bacteria. The study medication can increase your risk of certain bacterial infections in the eye; until now this risk is not observed in previous studies with the study medication in animals or humans. The injection of the study medication in the eye can also cause side effects. In these cases it concerns detachment of the retina of the underlying pigment layer or clouding of the lens (cataract), or temporary loss of vision due to an increase in the pressure within the eye. In a few patients, release of ocular fluid by a needle was necessary to reduce the eye pressure and resolve the temporary vision loss.

For further information see addendum 2 of the patient information

## Contacts

**Public**
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Beneluxlaan 2a
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NL
**Scientific**
Roche Nederland B.V.

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Woerden 3446 GR
NL

## Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

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

## Inclusion criteria

- Willingness and the ability to provide signed informed consent; additionally, at U.S. sites, patients must provide Health Insurance Portability and Accountability Act (HIPAA) authorization, and in other countries, as applicable according to national laws.
- Participants aged >= 50 years.
Ocular Inclusion Criteria: Study Eye.
- Well demarcated area(s) of GA secondary to AMD with no evidence of prior or active choroidal neovascularization (CNV)
- BCVA letter score superior or equal to 49 letters (Snellen equivalent of 20/100 or better) using ETDRS at starting distance of 4m
- If BCVA letter score is superior or equal to 79 letters (Snellen equivalent of 20/25 or better), at least one GA easion must be within 250 micrometers of the foveal centre.

## Exclusion criteria

GA Characteristics Exclusion Criteria
- GA in either eye due to causes other than AMD (monogenetic macular dystrophies [e.g., Stargardt disease, cone rod dystrophy] or toxic
maculopathies [e.g., chloroquine/hydroxychloroquine maculopathy]);Ocular Exclusion Criteria: Study Eye
- History of vitrectomy surgery, submacular surgery, or any other surgical intervention for AMD
- Previous laser photocoagulation for CNV, diabetic macular edema, retinal vein occlusion, and proliferative diabetic retinopathy
- Prior treatment with Visudyne®, external-beam radiation therapy (for intraocular conditions), or transpupillary thermotherapy
- History of prophylactic subthreshold laser treatment for AMD
- Previous intravitreal drug delivery (e.g., intravitreal corticosteroid injection, anti-angiogenic drugs, anti-complement agents, or device
implantation). A single intraoperative administration of a corticosteroid during cataract surgery for cystoid macular edema prophylaxis at least 3
months prior to screening is permitted.;Ocular Exclusion Criteria: Non-study eye

- Non-functioning non-study eye defined as either: BCVA of hand motion or worse OR no physical presence of non-study eye
(i.e., monocular);Ocular Exclusion Criteria: Both eyes
- Previous participation in interventional clinical trials for geographic atrophy or dry AMD (except of vitamins and minerals) irrespective of the
route of administration (ocular or systemic)
- Previous treatment with eculizumab, lampalizumab, fenretidine or any other drugs for geographic atrophy or dry AMD treatment;Concurrent Systemic Conditions Exclusion Criteria
- Uncontrolled blood pressure (defined as systolic >180 mm Hg and/or diastolic >110 mm Hg while patient is sitting) If a patient's initial
measurement exceeds these values, a second reading may be taken 30 or more minutes later. If the patient's blood pressure must be
controlled by anti hypertensive medication, the patient can become eligible if medication is taken continuously for at least 30 days prior to
Day 1.
- History of other diseases, metabolic dysfunction, physical examination finding, or clinical laboratory finding that gives reasonable suspicion of a
disease or condition that contraindicates the use of lampalizumab or that might affect interpretation of the results of the study or that renders the
patient at high risk of treatment complications
- Treatment for active systemic infection or localized infection. The ongoing prophylactic use of antimicrobial therapy should be discussed
with the Medical Monitor.
- Predisposition or history of increased risk of infection
- Active malignancy within past 12 months except for appropriately treated carcinoma in situ of the cervix, non-melanoma skin carcinoma
and prostate cancer with a Gleason score of < 6 and a stable prostate specific antigen (PSA) for > 12 months.
- History of allergy to fluorescein that is not amenable to treatment
- History of a severe allergic reaction or anaphylactic reaction to a biologic agent or known hypersensitivity to any component of the
lampalizumab injection
- Inability to comply with study or follow-up procedures
- Inability to obtain CFP, FAF, and FA of sufficient quality to be analyzed and graded by the central reading center
- Previous participation in any studies of investigational drugs within 3 months (except as listed in protocol section 4.1.2d) preceding Day 1
(excluding vitamins and minerals)

## Study design

## Design

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|---|---|
| Study phase: | 3 |
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Double blinded (masking used) |
| Control: | Placebo |
| Primary purpose: | Diagnostic |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 14-12-2015 |
| Enrollment: | 10 |
| Type: | Actual |

## Medical products/devices used

| | |
|---|---|
| Product type: | Medicine |
| Brand name: | NVT |
| Generic name: | lampalizumab |

# Ethics review

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|---|---|
| Approved WMO Date: | 11-12-2014 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 29-06-2015 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 10-08-2015 |
| Application type: | Amendment |

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| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 19-08-2015 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 02-10-2015 |
| 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: | 23-12-2015 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 26-02-2016 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 28-06-2016 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 28-07-2016 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 11-08-2016 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 15-08-2016 |
| Application type: | Amendment |

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|---|---|
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 07-07-2017 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 22-08-2017 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 20-09-2017 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 19-10-2017 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 15-12-2017 |
| Application type: | Amendment |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 22-12-2017 |
| 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 |
|---|---|
| EudraCT | EUCTR2014-000106-35-NL |
| ClinicalTrials.gov | NCT02247531 |
| CCMO | NL42319.018.14 |