A MULTICENTER, OPEN-LABEL EXTENSION STUDY TO EVALUATE THE LONG-TERM SAFETY AND TOLERABILITY OF LAMPALIZUMAB IN PATIENTS WITH GEOGRAPHIC ATROPHY SECONDARY TO AGE-RELATED MACULAR DEGENERATION WHO HAVE COMPLETED A ROCHE-SPONSORED STUDY

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The primary objective of this study is to evaluate the long-term safety and tolerability of ITV injections of 10 mg lampalizumab administered to patients with GA secondary to AMD as assessed by the:• Incidence and severity of ocular adverse events•...

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

Summary

ID

NL-OMON46297

Source
ToetsingOnline

Brief title
Omaspect/ GX30191

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: Lampalizumab, Macular degeneration, open label extention, Phase IIIb

Outcome measures

Primary outcome

• Incidence and severity of ocular adverse events

• Incidence and severity of systemic (non-ocular) adverse events

Secondary outcome

not applicable

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) and an exudative or wet form. 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 and those 70 years of age is 0.70% and rises to 2.91% and 11.29% for those 80 years of age and 90 years of age, respectively.

GA causes progressive damage to the macula, the central region of the retina (inside the eye), which is involved in seeing the fine details associated with reading, driving, and recognizing faces. In the advanced stage of the disease,

GA results in severe central vision loss, which impairs performance of many activities of daily living. The cause of AMD is not well understood. However, recent scientific studies have found that people with specific inherited (genetic) characteristics have an increased risk of AMD. Other scientific studies also suggest that an increased activation of a specific part of your immune system called the *alternative complement pathway* may be involved in the disease.
Currently, there is no approved treatment for GA. Lampalizumab, the study drug, is designed to slow down the activation of the alternative complement pathway and is given by intravitreal (the route of administration) injection into the eye.

Results from the Phase II Study CFD4870g provide evidence that lampalizumab may slow the progression of GA and that lampalizumab administered as 10-mg ITV injections monthly over 18 months demonstrates an acceptable safety and tolerability profile in patients with GA secondary to AMD. The open label Omaspect studie GX30191, will evaluate the long-term safety and tolerability of 10 mg lampalizumab administered by ITV injection to patients with GA secondary to AMD who have completed study treatment and the Week 96 visit in one of the parent studies (Study GX29176 or GX29815).
See protocol paragraphe 1.4 page 18.

See protocol chapter 1 page 16-18.

Study objective

The primary objective of this study is to evaluate the long-term safety and tolerability of ITV injections of 10 mg lampalizumab administered to patients with GA secondary to AMD as assessed by the:
• Incidence and severity of ocular adverse events
• Incidence and severity of systemic (non-ocular) adverse events

EXPLORATORY OBJECTIVES
• GA area progression (as measured by fundus autofluorescence [FAF])
• Change in clinical outcomes (as outlined below)
• Correlation between GA area progression and change in clinical outcomes
The clinical and patient-reported outcomes (PROs) included in this study are the following:
• Best corrected visual acuity (BCVA) score, as measured using the Early Treatment
Diabetic Retinopathy Study (ETDRS) chart (at a starting distance of 4 meters)
• BCVA score, as measured using ETDRS chart at a starting distance of 4 meters under low-luminance conditions
• Binocular and monocular reading speed, critical print size, and reading acuity, as
assessed using the Minnesota Low-Vision Reading Test (MNRead) or by Radner Reading Charts

• Patient-reported visual function, as assessed using the National Eye Institute Visual Functioning Questionnaire 25-item Version (NEI VFQ-25), particularly the NEI VFQ-25 composite score, the near activity subscale score, and the distance activity subscale score
• Patient-reported functional reading independence, as assessed using the Functional Reading Independence (FRI) Index score
• In a selected subset of patients, macular functional response, as assessed by mesopic microperimetry and measured by the number of scotomatous points and change in macular sensitivity- NA for sites in The Netherlands

At the discretion of the Sponsor, additional assessments may be included in this OLE (open label extention) study (Study GX30191), in which case a supplemental assessment protocol will be provided.

PHARMACOKINETIC OBJECTIVES
The pharmacokinetic (PK) objective for this study is to observe the systemic trough concentrations of 10 mg lampalizumab administered by ITV injections through the analysis of the serum lampalizumab concentrations. The exploratory PK objectives for this study are to observe the aqueous humor (optional sample) concentrations of lampalizumab and to explore possible relationships between lampalizumab PK, biomarkers, and clinically related endpoints.

IMMUNOGENICITY OBJECTIVES
The immunogenicity objective for this study is to evaluate the immune response to lampalizumab through the analysis of the incidence of anti-therapeutic antibodies (ATAs) during the study relative to the prevalence of ATAs at baseline.
The exploratory immunogenicity objective for this study is to evaluate potential effects of ATAs on the efficacy, safety, biomarker or PK endpoints.

BIOMARKER OBJECTIVE
The biomarker objective of this study is to explore the relationship of biomarkers to each other and to the endpoints in the study. These biomarkers include genetic variants identified in patients who completed the Phase III studies GX29176 and GX29185, candidate anatomic biomarkers identified by spectral domain*optical coherence tomography (SD-OCT), levels in the blood of proteins in the complement pathway, and molecular biomarkers measured in the optional aqueous humor sample. See the separate patient information RCR and protocol appendix 19 page 125 and Schedule of assessments appendix 1 pages 65-78.

See for more information protocol chapter 2 page 19-20.

In this open label extension study, patients will receive lampalizumab by intravitreal injection either every 4 weeks (Q4W) or every 6 weeks (Q6W). Lampalizumab is an experimental drug, which means that health authorities have not approved lampalizumab for the treatment of GA.

Study design

Omaspect is a multicenter, open-label extension study to evaluate the long-term safety and tolerability of lampalizuman in patients with geographic atrophy secondary to age-related macular degeneration who have completed a roche-sponsored study (GX29176 Chroma or GX29185 Spectri, named parent studies). Patients in the parent studies who discontinued from study treatment prior to completion of the 96-week treatment period are not eligible for enrollment in this extension study. The extension study will enroll two groups of patients from the parent studies: patients previously exposed to lampalizumab as well as patients who are lampalizumab-naïve (i.e., received sham during a parent study). Although this extension study is open-label, patients will remain masked to their previous treatment assignment in the parent study. Week 96 visit will serve as the final visit for the parent study and the Day 1 visit for the extension study (i.e., the two visits will be conducted on the same day). Patients must satisfy all eligibility criteria at the Day 1 visit. All patients from the parent studies who enroll in the OLE study will receive 10-mg ITV injections of lampalizumab. The study eye for the extension study will be the same eye that received lampalizumab or sham administrations in the parent study; only the study eye will receive administration of lampalizumab in this extension study. Dosing frequency in this extension study will remain consistent with the original dosing schedule in the parent study: thus either on the Q4W (± 5 days) schedule or the Q6W schedule (± 5 days).

See protocol chapter 3, pages 20-22.

Intervention

Patients that are participating are being treated with lampalizumab in a Q4W or Q6W dosing schedule.

Study burden and risks

The patient may have side effects from the drugs or procedures used in this study. Side effects can vary from mild to very serious and may vary from person to person. Everyone taking part in the study will be watched carefully for any side effects. However, Roche, the study doctor, and other doctors do not know all of the side effects that could occur. The study doctors may give

the patient drugs to help lessen side effects, and the patient may need to temporarily or permanently stop taking lampalizumab. Many side effects go away soon after you stop what is causing them. In some cases, side effects can be serious and may be long lasting or may never go away. There may even be a risk of death.
In a completed study, patients with GA received injections either monthly or every other month in an 18-month treatment period. The experience in that study suggests the administration of lampalizumab injections over time was well tolerated. Potential side effects of the study drug and related procedures are described below.

SIDE EFFECTS KNOWN TO BE ASSOCIATED WITH LAMPALIZUMAB AND/OR EYE INJECTION
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 the 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 (Occurring 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
• Eye pain

Common (Occurring 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 (Occurring in at least 1 in 1000 to 1 in 100 patients treated):
• A serious eye infection called endophthalmitis

SIDE EFFECTS POTENTIALLY ASSOCIATED WITH LAMPALIZUMAB AND/OR EYE INJECTION
EYE-RELATED COMPLICATIONS
There is a chance that the patients vision may worsen, which may result from progression of the eye disease, as a side effect of the study drug injections or for other reasons. The study drug may have the potential to cause inflammation in the eye, which may be experienced as redness, swelling, or pain in the eye. This inflammation may not be related to bacteria. The study drug may also increase the risk of having certain types of bacterial infections inside the eye; however, this risk has not been observed in previous animal or human studies with the study drug to date.
The injection of study drug into the eye also has the potential to cause side effects. These events include separation of the retina from the underlying pigment cell layer or a cloudiness of the eye 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.

The patient may experience side effects from the drugs or procedures used in this study. These may be associated with the use of lampalizumab, eye injection, drug-drug interaction, allergic reactions, possible risk and discomfort associated with drawing blood, risks of fluorescein angiography, bleeding associated with the use of blood-thinning medications, possible risks associated with loss of privacy and reproductive risks. These are described in the subject information leaflet.
See for (potential) side-effects the subject information leaflet and the IB.

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

• Willingness and 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.
• Willingness and ability to undertake all scheduled visits and assessments
• Previous enrollment in and completion of study treatment and the Week 96 visit of either Study GX29185 or Study GX29176, without early treatment discontinuation (lampalizumab or sham)
• For women of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraceptive methods with a failure rate of < 1% per year during the treatment period and for at least 30 days after the last dose of lampalizumab.
See for details protocol page 23-24
• For men: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraceptive measures, and agreement to refrain from donating sperm.
See for details protocol page 24
• For patients participating in microperimetry (at selected sites only): must have participated in the microperimetry testing during the parent study (Chroma en Spectri) - Sites in The Netherlands are not participating in the microperimetry study

Exclusion criteria

• Concurrent ocular conditions exclusion criterion
History of other ocular diseases that give 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
• Concurrent systemic conditions exclusion criteria
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;
Predisposition to or history of increased risk of infection (see Section 4.1.2 of the protocol);
Requirement for continuous use of any medications or treatments indicated in the *Excluded Therapy* section of the protocol (see Section 4.4.2)
Pregnancy or lactation, or intention to become pregnant during the study (see Section 4.1.2 of the protocol).

Study design

Design

Study phase: 3

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-08-2017
Enrollment:	2
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	lampalizumab

Ethics review

Approved WMO Date:	19-04-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	21-07-2017
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-08-2017
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:	21-12-2017
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	EUCTR2016-000423-13-NL
ClinicalTrials.gov	NCT02745119
CCMO	NL61473.018.17