A Phase 3, Multi-Center, Randomized, Double-Masked, Sham-Controlled Study to Compare the Efficacy and Safety of Intravitreal Pegcetacoplan Therapy with Sham Injections in Patients with Geographic Atrophy (GA) Secondary to Age-Related Macular Degeneration (AMD)

Published: 31-10-2018
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Primary To evaluate the efficacy of Pegcetacoplan compared to sham injection in patients with GA secondary to AMD assessed by change in the total area of GA lesions from baseline as measured by FAF.Key SecondaryTo evaluate the efficacy of...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Ocular structural change, deposit and degeneration NEC
Study type	Interventional

Summary

ID

NL-OMON55547

Source
ToetsingOnline

Brief title
OAKS

Condition

- Ocular structural change, deposit and degeneration NEC

Synonym
Age-Related Macular Degeneration, retinal aging

Research involving
Human

Sponsors and support

Primary sponsor: Apellis Pharmaceuticals Inc.
Source(s) of monetary or material Support: Apellis Pharmaceuticals Inc.

Intervention

Keyword: Age-Related Macular Degeneration (AMD), Geographic Atrophy (GA), Intravitreal injections, Pegcetacoplan

Outcome measures

Primary outcome

Primary Efficacy Endpoint

• Change from baseline to Month 12 in total area of GA lesion(s) in the study

eye (in mm2) based on Fundus Autofluorescence (FAF).

Secondary outcome

Key Secondary Efficacy Endpoints

• Change from baseline in monocular maximum reading speed (study eye), as

assessed by Minnesota Reading (MNRead) or Radner Reading Charts at Month 24 (in

select countries)

• Change from baseline in Functional Reading Independence (FRI) index score, at

Month 24.

• Change from baseline in normal luminance best-corrected visual acuity score

(NL-BCVA) at Month 24 as assessed by ETDRS chart.

Study description

Background summary

Age-related macular degeneration is the leading cause of severe vision loss in people over the age of 65 in the United States and other Western countries. While there is treatment for exudative AMD with anti-VEGF therapies, no approved therapy exists for GA which is usually bilateral and relentlessly progressive. It represents a significant unmet need as it leads to significant visual impairment and affects more than 5 million people worldwide. Human biochemical, genetic, and clinical lines of evidence indicate that the complement system plays a role in the etiology of age-related macular degeneration (AMD). Pegcetacoplan is a PEGylated cyclic peptide inhibitor of complement C3. The peptide portion of the drug binds to complement C3 and is a broad inhibitor of the complement cascade, a biological process that is part of innate immunity and is involved in multiple inflammatory processes. The PEGylation of the molecule imparts slower clearance from the vitreous humor following administration. If efficacious, Pegcetacoplan is expected to alter the course of GA and slow its rate of progression.

Study objective

Primary
To evaluate the efficacy of Pegcetacoplan compared to sham injection in patients with GA secondary to AMD assessed by change in the total area of GA lesions from baseline as measured by FAF.

Key Secondary
To evaluate the efficacy of Pegcetacoplan compared to sham-injection in patients with GA secondary to AMD with respect to:
o Monocular maximum reading speed (study eye), as assessed by Minnesota Reading or Radner Reading (MNRead) Charts (in select countries)
o Functional Reading Independence (FRI) index score
o Normal luminance best-corrected visual acuity score (NL BCVA) in the study eye

Study design

This is a 30-month, Phase III, multicenter, randomized, double-masked, sham-injection controlled study to assess the efficacy and safety of multiple IVT injections of Pegcetacoplan in subjects with GA secondary to AMD.
The study will randomize approximately 600 subjects across approximately 100 multinational sites. Subjects will be screened within 28 days before receiving Pegcetacoplan or Sham injection. Upon entry into the study, subjects will be assigned a screening number. Subjects who meet all inclusion and none of the

exclusion criteria will return to the clinic for randomization and treatment on Visit 2 (Day 1). At this visit, subjects will be randomized 2:2:1:1 to receive APL-2 Monthly, APL-2 Every-Other-Month, Sham injection Monthly or Sham-injection Every-Other-Month, respectively. Randomization will be stratified according to GA lesion area at screening (< 7.5 mm2; >= 7.5 mm2), and presence of CNV in the fellow eye.
All subjects will be assessed monthly during the first 12 months regardless of treatment regimen. From Month 12 to Month 24, subjects will follow the outlined visit schedule (45TAppendix A45T to 45TD45T) based on treatment assignment (i.e. subjects in the monthly groups will be assessed monthly while subjects in the every-other-month will be assessed every-other-month). Subjects will be offered entry into an open-label extension study at the end of the 24-month treatment period.

Intervention

Pegcetacoplan intravitreal injections or sham injections

Study burden and risks

Although the subjects receiving Pegcetacoplan might be at a risk of developing wet AMD, this can be treated with standard of care anti-VEGF therapies. Furthermore, the ophthalmic procedures required for participants in this study might have some risks as well, but these procedures are all standard and widely performed in ophthalmology.
As there is a potential health benefit for trial participants from receipt of study drug, i.e. an altered course of GA and slow down of the AMD progression. This potential health benefits outweighs the risks associated with participation in this study.

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

1. Age >= 60 years.
2. NL-BCVA of 24 letters or better using ETDRS charts.
3. Clinical diagnosis of GA of the macula secondary to AMD as determined by the Investigator and confirmed by the Reading Center.
4. The GA lesion must meet the criteria as determined by the central reading center*s assessment of FAF imaging at screening.
5. Adequate clarity of ocular media, adequate pupillary dilation, and fixation to permit the collection of good quality images as determined by the Investigator.
6. Meets the criteria related to microperimetry.
7. Female subjects must be women of non-child-bearing potential or women of child-bearing potential with a negative pregnancy test at screening and must agree to use protocol defined methods of contraception.
8. Males with female partners of child-bearing potential must agree to use protocol defined methods of contraception
9. Willing and able to give informed consent and to comply with the study procedures and assessments.

Exclusion criteria

1. GA secondary to a condition other than AMD such as Stargardt disease, cone rod dystrophy or toxic maculopathies like plaquenil maculopathy in either eye.
2. Spherical equivalent of the refractive error demonstrating > 6 diopters of myopia or an axial length >26 mm.
3. Any history or active CNV, associated with AMD or any other cause, including any evidence of retinal pigment epithelium rips or evidence of neovascularization anywhere based on SD-OCT imaging and/or fluorescein

angiography as assessed by the Reading Center.
4. Presence in either eye of an active ocular disease that in the opinion of the Investigator compromises or confounds visual function, including but not limited to, uveitis, other macular diseases (e.g. clinically significant epiretinal membrane (ERM), full thickness macular hole or uncontrolled glaucoma/ocular hypertension. Benign conditions in the opinion of the investigator such as peripheral retina dystrophy are not exclusionary).
5. Intraocular surgery (including lens replacement surgery) within 3 months prior to randomization.
6. History of laser therapy in the macular region.
7. Aphakia or absence of the posterior capsule. Note: YAG laser posterior capsulotomy for posterior capsule opacification done at least 60 days prior to screening is not exclusionary.
8. Any ocular condition other than GA secondary to AMD that may require surgery or medical intervention during the study period or, in the opinion of the Investigator, could compromise visual function during the study period
9. Any contraindication to IVT injection including current ocular or periocular infection
10. History of prior intravitreal injection in the study eye.
11. Unable to perform microperimetry reliably in the opinion of the investigator.
12. Prior participation in another interventional clinical study for intravitreal therapies in either eye (including subjects receiving sham).
13. Prior participation in another interventional clinical study for geographic atrophy in either eye including investigational oral medication and placebo.
14. Participation in any systemic experimental treatment or any other systemic investigational new drug within 6 weeks or 5 half-lives of the active (whichever is longer) prior to the start of study treatment.
15. Medical or psychiatric conditions that, in the opinion of the investigator, make consistent follow-up over the 24-month treatment period unlikely, or would make the subject an unsafe study candidate.
16. Any screening laboratory value (hematology, serum chemistry or urinalysis) that in the opinion of the Investigator is clinically significant and not suitable for study participation.
17. Known hypersensitivity to fluorescein sodium for injection or hypersensitivity to Pegcetacoplan or any of the excipients in Pegcetacoplan solution.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	17-12-2019
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	na
Generic name:	Pegcetacoplan

Ethics review

Approved WMO Date:	31-10-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-04-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-06-2019
Application type:	First submission

Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-10-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-10-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	15-06-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	19-06-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-10-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-11-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	06-04-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-04-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-05-2021
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-11-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-05-2022
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	EUCTR2018-001435-52-NL
ClinicalTrials.gov	NCT03525613
CCMO	NL67314.018.18