A phase 3, open-label, multicenter, extension study to evaluate the long-term safety and efficacy of Pegcetacoplan in subjects with geographic atrophy secondary to age-related macular degeneration

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This study has been transitioned to CTIS with ID 2024-512945-18-00 check the CTIS register for the current data. Objectives:Primary: To evaluate the long-term safety of IVT injected pegcetacoplanSecondary:1. To assess changes in the total area of...

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

Summary

ID

NL-OMON54299

Source
ToetsingOnline

Brief title
APL2-GA-305 / GALE study

Condition

- Ocular structural change, deposit and degeneration NEC

Synonym
Age-Related Macula 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), Long-term extension study, Pegcetacoplan intravitreal injections

Outcome measures

Primary outcome

Endpoints:

Primary:

• Incidence and severity of ocular and systemic adverse events (time frame: up

to 36 months)

Secondary outcome

Secondary:

Change from baseline in the following parameters:

• The total area of GA lesion(s) in the study eye (in mm2) as assessed by FAF

at month 12, month 24, and month 36

• The rate of change in GA lesion growth in the study eye as assessed by FAF at

month 12, month 24, and month 36

• NL-BCVA score (study eye) as assessed by Early Treatment Diabetic Retinopathy

Study (ETDRS) chart at month 12, month 24, and month

• LL-BCVA score (study eye) as assessed by ETDRS chart at month 12, month 24,

and month 36

• Monocular maximum reading speed (study eye), corrected for the number of

words read incorrectly, as assessed by Minnesota Reading (MNRead) charts or Radner charts at month 12, month 24, and month 36

• Binocular maximum reading speed, corrected for the number of words read incorrectly, as assessed by MNRead charts or Radner charts at month 12, month 24, and month 36

• The number of scotomatous points (study eye) assessed by mesopic microperimetry (selected participants [those who had the assessment performed in the antecedent study] only) at month 12, month 24, and month 36

• Macular sensitivity (study eye) as assessed by mesopic microperimetry (selected participants [those who had the assessment performed in the antecedent study] only) at month 12, month 24, and month 36

• Change in additional microperimetry parameters in the study eye (eg, 95% bivariate contour ellipse area [BCEA], number of points with a clinically significant decrease in mean sensitivity) at month 12, month 24, and month 36

• Mean Functional Reading Independence (FRI) Index score at month 12, month 24, and month 36

• National Eye Institute Visual Functioning Questionnaire 25-Item Version (NEI VFQ-25 and NEI VFQ-39 [at selected sites]) composite score, near activity subscale score, distance activity subscale score, and NEI VFQ-25 driving subscale score at month 12, month 24, and month 36

Safety:

• Presence of antibodies to the PEG and/or peptide moiety of pegcetacoplan

(time frame: up to 36 months)

• Incidence of new active choroidal neovascularization in the study eye as

assessed by FA at month 12, month 24, and month 36

• Incidence and severity of ocular and systemic adverse events (time frame: up

to 36 months) of participants being treated bilaterally with pegcetacoplan

Study description

Background summary

At this time, there is no effective treatment available for geographic atrophy secondary to age-related macular degeneration. Patients with geographic atrophy generally lose vision due to death of cells in the retina. The regions of dead cells are called GA lesions. This study is being done to see if the drug pegcetacoplan may be able to slow down growth of the GA lesion.

Study objective

This study has been transitioned to CTIS with ID 2024-512945-18-00 check the CTIS register for the current data.

Objectives:
Primary: To evaluate the long-term safety of IVT injected pegcetacoplan
Secondary:
1. To assess changes in the total area of geographic atrophy (GA) lesion in the study eye measured by fundus autofluorescence (FAF).
2. To assess changes in visual function as measured by:
a. Normal-luminance best-corrected visual acuity score (NL-BCVA) in the study eye
b. Low-luminance best-corrected visual acuity score (LL-BCVA) in the study eye
c. Reading speed in the study eye
3. To assess the macular functional response as assessed by mesopic microperimetry in the study eye (selected participants [those who had the assessment performed in the antecedent study] only).
4. To evaluate changes in participant-reported outcomes as measured by:
a. National Eye Institute Visual Functioning Questionnaire 25 Item Version (NEI VFQ-25)
b. Functional Reading Independence (FRI) Index

Study design

Overall Study Design:
This is a phase 3, multicenter, 36-month, open-label extension study to assess the safety and efficacy of long-term IVT injections of pegcetacoplan in participants with GA secondary to age-related macular degeneration (AMD). The study will enroll approximately 1200 participants across approximately 250 multinational sites who previously participated in a study evaluating pegcetacoplan for GA. Screening can happen on the same day as the last visit in the antecedent study or within 60 days of the last visit. Participants who meet all inclusion and none of the exclusion criteria will be included in this study. Participants will receive monthly pegcetacoplan treatment in the study eye if they were in the monthly treatment group (pegcetacoplan or sham) in the antecedent study. Participants will receive EOM pegcetacoplan treatment in the study eye if they were in the EOM treatment group (pegcetacoplan or sham) in the antecedent study. The study eye will be the same eye as the study eye of the antecedent study.

Participants who previously developed exudative AMD in the study eye in the antecedent study and are currently receiving anti-vascular endothelial growth factor (VEGF) therapy are eligible to participate in this extension study and will continue to receive pegcetacoplan. Participants who developed exudative AMD in the parent study or in this extension study will remain in the study and may also receive anti VEGF in addition to pegcetacoplan based on the investigator assessment following standard of care.

Participants who permanently discontinue pegcetacoplan in the study eye will also be terminated from the study. Participants who discontinue the study should complete the early termination visit.

The fellow eyes with GA that meet certain criteria are allowed to receive treatment with pegcetacoplan when the treating physician and participant deem beneficial. The treatment regimen (monthly or EOM) should be decided by the investigator.

Intervention

Pegcetacoplan, 15 mg/100 µL (monthly or every other month [EOM]), intravitreal (IVT) injections
Participants will receive monthly pegcetacoplan treatment if they were in the monthly treatment group (pegcetacoplan or sham) in the antecedent study.
Participants will receive EOM pegcetacoplan treatment if they were in the EOM treatment group (pegcetacoplan or sham) in the antecedent study. The study eye will be the same eye as the study eye of the antecedent study.
Participants who previously developed exudative AMD in the study eye in the antecedent study and are currently receiving anti-vascular endothelial growth factor (VEGF) therapy are eligible to participate in this extension study and will continue to receive pegcetacoplan. Participants who developed exudative AMD in the parent study or in this extension study will remain in the study and

may also receive anti-VEGF in addition to pegcetacoplan based on the investigator assessment following standard of care.
Participants who permanently discontinue pegcetacoplan will also be terminated from the study. Participants who discontinue the study should complete the early termination visit.

Study burden and risks

Participants who previously developed exudative AMD in the study eye in the antecedent study and are currently receiving anti-vascular endothelial growth factor (VEGF) therapy are eligible to participate in this extension study and will continue to receive pegcetacoplan. Participants who developed exudative AMD in the parent study or in this extension study will remain in the study and may also receive anti-VEGF in addition to pegcetacoplan based on the investigator assessment following standard of care.
Since there is a possible potential health benefit for participants receiving the study drug, this could be an altered course of GA and slower progression of AMD, the benefits outweigh the risks associated with participating in this study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Ocular-specific inclusion criteria apply to the study eye.
1. Participated in APL2-103 (NCT03777332) or completed the treatment at month 24 of either APL2-303 (Derby, NCT03525613) or APL2-304 (Oaks, NCT03525600). Specifically, for the APL2-303 and APL2-304 studies, the following criterion also applies:
a. Participants who did not permanently discontinue treatment but missed the month 24 visit are also eligible to participate in this extension study; however, to be eligible, these subjects must be screened within 60 days from the last day of the expected month 24 visit window for the antecedent study.
2. Clarity of ocular media, adequate pupillary dilation, and fixation to permit the collection of good quality images as determined by the investigator.
3. Female participants must be:
a. Women of nonchildbearing potential, or
b. Women of childbearing potential with a negative serum pregnancy test at screening and must agree to use protocol defined methods of contraception for the duration of the study and 90 days after their last dose of pegcetacoplan, and refrain from breastfeeding for the duration of the study.
4. Males with female partners of childbearing potential must agree to use protocol defined methods of contraception and agree to refrain from donating sperm for the duration of the study and for 90 days after their last dose of pegcetacoplan.
5. Willing and able to give informed consent and to comply with the study procedures and assessments.

Fellow Eye Inclusion Criteria
The following inclusion criterion applies to the fellow eye:
2. Clarity of ocular media, adequate pupillary dilation, and fixation to permit the collection of good quality images as determined by the investigator.

Exclusion criteria

Ocular-specific exclusion criteria apply to the study eye.
1. Participants who permanently discontinued the study drug prior to month 24 in the APL2-303 or APL2-304 studies and remained only for safety assessments. Temporary pause of the study drug is not exclusionary.
2. Presence of an active ocular disease that, in the opinion of the

investigator, compromises or confounds visual function, including, but not limited to, macular hole or other macular diseases (eg, clinically significant epiretinal membrane). Benign conditions in the opinion of the investigator such as peripheral retinal dystrophy are not exclusionary.
3. Any contraindication to IVT injection including current ocular or periocular infection.
4. Medical or psychiatric condition that, in the opinion of the investigator, is clinically significant and not suitable for study participation or make consistent follow-up over the 36-month treatment period unlikely.
5. Known hypersensitivity to fluorescein sodium for injection or hypersensitivity to pegcetacoplan or any of the excipients in pegcetacoplan solution.
6. Pregnancy, breastfeeding, or positive pregnancy test.

Fellow Eye Exclusion Criteria
The following exclusion criteria apply to the fellow eye:
2. Presence of an active ocular disease that, in the opinion of the investigator, compromises or confounds visual function, including, but not limited to, macular hole or other macular diseases (eg, clinically significant epiretinal membrane). Benign conditions in the opinion of the investigator such as peripheral retinal dystrophy are not exclusionary.
3. Any contraindication to IVT injection including current ocular or periocular infection.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-03-2022
Enrollment:	4
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	na
Generic name:	Pegcetacoplan

Ethics review

Approved WMO Date:	01-06-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	17-09-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-01-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	01-05-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	16-05-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-08-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	24-08-2022
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-03-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl
Approved WMO Date:	24-03-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl
Approved WMO Date:	26-03-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389

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Approved WMO Date:	04-12-2023
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl
Approved WMO Date:	29-03-2024
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389 mecamc@amsterdamumc.nl
Approved WMO Date:	18-04-2024
Application type:	Amendment
Review commission:	MEC Academisch Medisch Centrum (Amsterdam) Kamer G4-214 Postbus 22660 1100 DD Amsterdam 020 566 7389

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Approved WMO Date:	24-05-2024
Application type:	Amendment
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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
EU-CTR	CTIS2024-512945-18-00
EudraCT	EUCTR2020-002931-32-NL
ClinicalTrials.gov	NCT04770545
CCMO	NL77278.018.21