Geographic Atrophy (GA)

**Designed for Patients**

1. Age ≥60 years
2. With a clinical diagnosis of GA secondary to age-related macular degeneration
3. With best corrected visual acuity (BVCA) of 24 letters (approximately 20/300 Snellen equivalent)
Geographic Atrophy (GA)

Geographic atrophy is an advanced form of age-related macular degeneration (AMD). This condition leads to permanent, growing “blind spots” within the center of the visual field. This vision loss makes daily activities such as reading, driving a car, or recognizing people’s faces very challenging.

- As a healthy person ages, clumps of debris from damaged cells may form in the retina. These clumps are called drusen and are the early sign of age-related macular degeneration (AMD).
- In patients with risk factors, there is a progressive accumulation of drusen leading to damage of the retina cells. This is the advanced form of AMD called Geographic Atrophy, also known as “dry” AMD.

Role of Complement in GA

The complement system is a part of the immune system. It plays an important role in removing unwanted debris from the body, however, the overactivation of the complement system can be damaging to the retina cells. There are several reasons to believe that overactivation of the complement system plays a role in the development of GA:

- People with a gene mutation that is known to lead to higher activation of the complement system are at high risk for dry AMD.
- Patients with AMD also have signs of complement activation in the blood.
- Signs of increased activation of the complement cascade have also been found post mortem in eye tissues of patients who had dry AMD.
The Derby and Oaks clinical trials will test APL-2 to see whether it is effective and safe for reducing the progression of AMD to GA.

By targeting C3 at the point of convergence of all complement activation pathways and upstream of C5, APL-2 can inhibit all 3 principal complement activation pathways. Thus, APL-2 may be more effective in a broad patient population than a partial inhibitor of complement would be.

Purpose of Derby & Oaks Clinical Trials

The Derby and Oaks clinical trials will test APL-2 to see whether it is effective and safe for reducing the progression of AMD to GA.

Key Inclusion Criteria

1. Age ≥60 years
2. Normal-Luminance Best Corrected Visual Acuity (NL-BCVA) of 24 letters or better on Early Treatment Diabetic Retinopathy Study (ETDRS) charts (~20/320 Snellen equivalent)
3. Clinical diagnosis of GA secondary to AMD
4. Fundus autofluorescence (FAF) imaging shows:
   a. Total GA area ≥2.5 and ≤17.5 mm² (1 and 7 disk areas [DA] respectively)
   b. If GA is multifocal, ≥1 focal lesion must be ≥1.25 mm² (0.5 DA), with the overall aggregate area of GA as specified in 4.a
   c. The entire GA lesion must be completely visualized on the macula-centered image and must be able to be imaged in its entirety, and not contiguous with any areas of peripapillary atrophy
   d. Presence of any pattern of hyperautofluorescence in junctional zone of GA
5. Adequate clarity of ocular media, adequate pupillary dilation, and fixation to permit the collection of good-quality images
**Key Exclusion Criteria**

1. GA secondary to a condition other than AMD
2. Spherical equivalent of the refractive error demonstrating >6 diopters of myopia or an axial length >26 mm
3. Any history or presence of active choroidal neovascularization (CNV), associated with AMD or any other cause in the study eye. Note: presence of CNV in the fellow eye is not exclusionary
4. Presence in either eye of an active ocular disease that confounds visual function
5. Intraocular surgery within 3 months prior to randomization
6. History of laser therapy in the macular region
7. Aphakia or absence of the posterior capsule
8. Any ocular condition other than GA secondary to AMD that may require surgery or medical intervention during the study period
9. Any contraindication to intravitreal injection
10. History of prior intravitreal injection in the study eye
11. Prior participation in another interventional clinical study for intravitreal therapies in either eye (including subjects receiving sham)

**Dosing of APL-2**

Subjects will be randomly assigned to receive treatment either monthly or every other month (EOM). Starting on day 1 of the treatment phase, all subjects will receive a single intravitreal dose of 15 mg APL-2/0.1 mL or a sham procedure either monthly or EOM (depending on treatment assignment) for a total of 24 months. The subjects assigned to monthly treatment will receive up to 25 injections, and the subjects assigned to EOM treatment will receive up to 13 injections.

**Study Visits**

- All subjects will be assessed monthly during the first 12 months, regardless of treatment regimen
- From month 12 to month 24, subjects in one group will be assessed monthly, while the subjects in the other group will be assessed every other month
- Additional follow-up safety assessments, without study drug administration, will be performed for all subjects at months 27 and 30

**Primary Efficacy Outcome Measure**

- Mean 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 Measures

- Mean change from baseline in:
  - Monocular reading speed (study eye), as assessed by Minnesota Reading (MNRead) Chart or Radner Reading Charts
  - Functional Reading Independence Index (FRII) composite score
  - NL-BCVA as assessed by ETDRS chart
  - Low-luminance BCVA as assessed by ETDRS chart
  - Low luminance deficit
  - The total area of GA lesion(s) in the study eye (in mm²), as assessed by FAF
  - Monocular critical print size (study eye), as assessed by MNRead or Radner Reading Charts
  - The National Eye Institute Visual Functioning Questionnaire 25-Item Version distance activity subscale score
- Systemic plasma concentration of APL-2 over time

Safety Outcome Measures

- Incidence and severity of ocular and systemic treatment-emergent adverse events
- Incidence of anti-therapeutic antibodies directed against APL-2
- Incidence of new active CNV in the study eye
Derby and Oaks Study Locations

These studies are being conducted at over 100 locations throughout the United States

To Recommend a Patient for This Trials, Email
apellisclinicaltrials@cherryhcc.com

or visit
https://GAstudies.com

References


