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CURRENT AND FUTURE MANAGEMENT OF GEOGRAPHIC ATROPHY

David Eichenbaum, MD; Carl Regillo, MD; and Lejla Vajzovic, MD

The next year may see significant changes in the geographic atrophy (GA) treatment landscape, as two companies, Iveric Bio and Apellis Pharmaceuticals, have each submitted New Drug Applications to the FDA for novel therapies targeting the role of complement inhibition—albeit by different strategies. To set the stage for what may be a transformative time in the lives of individuals affected by GA secondary to dry AMD, YoungMD Connect invited a panel of noted retina specialists to offer perspective on the current clinical landscape, what it means to live with a GA diagnosis (Figure), and why the development pipeline offers hope for optimism.

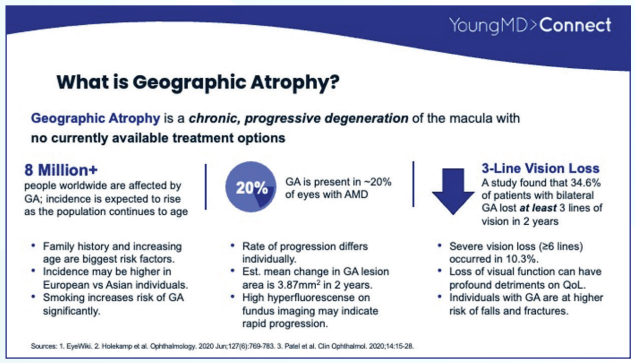

Figure. Fast facts about geographic atrophy.

SETTING THE STAGE: THE PATIENT PERSPECTIVE

David Eichenbaum, MD

"It's a bit of a helpless feeling for the physician to have to explain the visual consequences of GA and then add that there are no currently available treatment options."

- Consulting with GA patients can be very frustrating for the patient, for their family and support network, and for the physician.
  - The need for routine monitoring only compounds the burden and effects on daily living that patients with GA experience.
  - GA patients are typically older, and many need help attending their appointments, making GA a burden to the family and support network.
- Although vision loss associated with GA occurs late in the disease, it can be devastating. The slow progression of a central scotoma is something understood clinically, but for patients, it means the world is slowly disappearing before their eyes.
  - Referral to low vision services is an "underutilized service that definitely helps patients use their remaining vision more effectively."
- There is a definite knowledge gap around GA, and that can be a barrier.
  - The term geographic atrophy is not really used much in optometry or general ophthalmology practice, so when these patients get to the retina specialists, it may be the first time they are hearing the term.

THE CURRENT LANDSCAPE: CLINICAL PERSPECTIVE OF GA

Lejla Vajzovic, MD

"The first complaint that our patients typically have is difficulty with night vision, which translates to difficulties with reading speed and doing activities they enjoy doing."

- Patient-reported symptoms will lead the retina specialist to get an OCT or fluorescein angiography (FA); however, these practices may not be routinely used in general ophthalmology or optometric practices.
  - OCT coupled with infrared fundus photography is more common.
  - Autofluorescence is the best way to identify and understand the extent of GA.
- Referral to low vision specialists is key. These services help patients change their environment or give them tools to help them use their existing vision more effectively.
  - While loss of visual acuity (VA) is associated with GA, it is likely not the first symptom patients notice. Instead, patients often experience of loss of visual function (ie, difficulty reading, driving) as the first noticeable sign.
  - VA is not affected until the end stage of GA—typically when GA reaches the macula. The loss of VA in end-stage GA is sometimes referred to as "falling off the cliff."
- A number of ongoing clinical trials are testing new agents; some may pan out while others may not work—does talking about them offer hope or potentially false promises?
  - Dr. Vajzovic believes that mentioning ongoing clinical trials as part of the education process may be worthwhile. Her institution does a lot of research, so bringing up clinical trials is partly about increasing enrollment; at the same time, offering hope about what is coming in the pipeline may get patients to buy in to the need for monitoring.

THE FUTURE IS BRIGHT: A LOOK DOWN THE INNOVATION PIPELINE

Carl Regillo, MD

"We're pushing the boulder uphill. The new agents in the pipeline represent significant progress and, if they make it to the clinic, would be meaningful for patients and their families."

- There are agents in the pipeline that have demonstrated an ability to reduce the rate of growth of GA, which could delay the time to vision loss.
  - As well, a reduction in a central scotoma might help the patient use low vision aides more effectively and for longer.
- Complement inhibition is the only strategy that has demonstrated therapeutic effect in GA in clinical trials; some of the key ones to be aware of:
  - C3 blocker - APL-2 (pegcetacoplan; Apellis)
    - Intravitreally injected; in phase 3 trials, pegcetacoplan reduced GA lesion growth compared to sham and demonstrated a favorable safety profile. It is currently being reviewed by the FDA.
  - C5 blocker - aptamer - Zimura (avacincaptad pegol; Iveric Bio)
    - Studied in GATHER 1 and 2 trials.
    - Recently released data showed a statistically significant reduction in mean rate of growth in GA area with a favorable safety profile.
  - Both of these agents have demonstrated small effects from a clinical perspective, but they are nonetheless significant: any improvement would be meaningful in the context of current unmet need.
  - Both phase 3 studies used an anatomic endpoint, and no studies in GA have shown an effect on VA to date.
    - It is important to note that VA loss associated with GA typically occurs late in the disease process.
- Several previous attempts at developing GA therapies have failed; the history of those programs may be important to understand for those ophthalmologists who may interact with GA patients in their clinic.