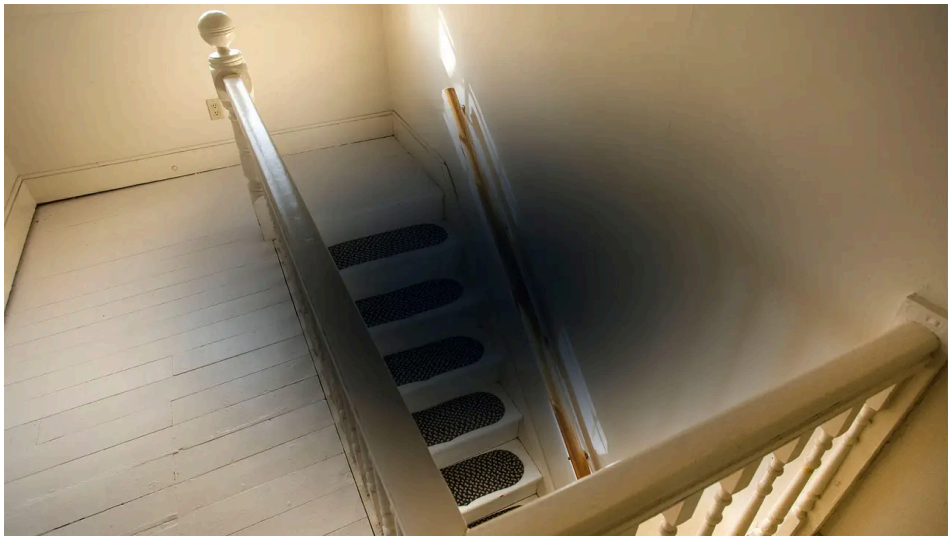
Honing the Indications for Treating Geographic Atrophy

— Better baseline vision, proximity to foveal center emerge as clues, but clinical value unclear

by Charles Bankhead, Senior Editor, MedPage Today
February 7, 2025



Geographic atrophy (GA) progressed more often in patients with better baseline vision and those with lesions closer to the foveal center, according to a study that could help provide needed treatment guidance.

Patients with a baseline best corrected visual acuity (BCVA) ≥40 letters and all GA lesions within 1 mm of the foveal center had significant vision loss averaging 11.33 letters at 4 years. In contrast, patients who met neither criterion did not have significant vision loss. Additionally, more rapid GA progression was associated with greater vision loss.

The findings could represent a step toward more personalized approaches to treatment and provide guidance in future clinical trial design, reported Lucian V. Del Priore, MD, PhD, of Yale School of Medicine in New Haven, Connecticut, and co-authors in *Ophthalmology*.

"Our results provide some guidance on treating GA patients with the recently approved intravitreal pegcetacoplan [Syfovre] and avacincaptad pegol [Izervay], as well as with future therapies that can slow GA progression," the authors stated in their discussion. "Since the approval of the two intravitreal complement inhibitors, there have been numerous debates on which GA patients should be treated. Although the phase III clinical trials have shown an approximately 20% reduction in GA growth rate, no significant improvement in functional outcomes has been observed in pre-specified analyses."

"The current decision to treat GA patients is left to the patient and individual physician's discretion," they added. "Consequently, there is a pressing need for further evidence-based guidelines to help physicians identify which patients might benefit most from these treatments. This requires a detailed understanding of the natural history of how GA affects visual function."

In the absence of additional informative data, the authors suggested a three-step evaluation of a patient for GA treatment:

- If BCVA is <40 letters, further decline over 4 years is unlikely, making treatment benefit less likely.
- If BCVA is ≥40 letters, evaluate GA proximity to the foveal center. Geographic atrophy >1 mm from the foveal center might be better suited for observation. Eyes with GA ≤1 mm from the foveal center and BCVA ≥40 letters will likely have significant BCVA loss

over 4 years, regardless of GA growth rate. Such eyes may benefit from treatment to slow GA.

- Optionally, measuring GA growth rate may help refine decision making. Eyes with rapid GA progression, good baseline BCVA, and GA involving or near the foveal center are most likely to benefit from treatment.

Importance Versus Applicability

The data, based on the AREDS and AREDS2 studies of the clinical course of age-related macular degeneration, are valuable but have limitations for current clinical practice, according to Jay Chhablani, MD, of the UPMC Vision Institute in Pittsburgh.

"Does it define us today, to decide which patient to offer treatment or not? I really doubt it," he told *MedPage Today*. "The data is based on color fundus photographs, and now we have a lot of evidence in terms of using OCT [optical coherence tomography] and getting much more information."

"I'm very glad that they came up with the exact number of less than 1 mm from the foveal center," Chhablani added. "So, they are trying to define the treatment plan, but I would say that we still will not be able to take this information to the clinic right away."

The data are unlikely to have a major impact on current clinical practice, seconded Richard Rosen, MD, of the Icahn School of Medicine at Mount Sinai in New York City.

"They have data on [a large number of patients] and they have long-term follow-up, so we can see, over time, whether some of our initial impressions bear fruit," said Rosen.

"A lot of the results are quite intuitive," he continued. "The patients who had better visual acuity and seemed to have more to lose, and ones where the geographic atrophy was closer to the fovea tended to progress more rapidly. Patients who had poor vision or had lesions that were farther in the macula from the fovea really didn't progress that quickly. That makes sense in terms of what I see clinically with these patients.... The results validate a lot of my clinical suspicions and clinical impressions from what I've seen, and it's always good to have that kind of validation."

Background, Key Findings

Del Priore and colleagues analyzed data for 1,351 eyes and 994 participants in the two AREDS studies, of whom 594 eyes from 464 participants had 4-year follow-up. They examined change in BCVA over 4 years and the relationship between decline in BCVA and baseline factors.

Baseline characteristics included a mean age of 75.7 years, mean BCVA of 67.5 letters, and mean GA area of 3.30 mm^2. Mean growth rate of square root-transformed GA was 0.30 mm/year.

Overall, mean BCVA declined by 8.86 letters from baseline to year 4, including -8.14 letters in eyes with central GA at baseline and -9.26 letters in eyes with non-central GA, a nonsignificant difference. Univariate analysis showed that

BCVA loss at 4 years had significant associations with higher baseline BCVA ($P<0.001$), multifocal GA at baseline ($P=0.002$), closer GA proximity to the foveal center ($P=0.003$), and faster GA progression ($P<0.001$). By multivariate analysis, all of the factors except multifocal GA remained significantly associated with BCVA vision loss at 4 years.

Refining the overall results, investigators examined 4-year change in BCVA as a function of baseline BCVA. Patients with baseline BCVA <40 letters (69 eyes, 69 patients) did not have a significant decline in BCVA at 4 years. The mean change in BCVA was +3.99 letters ($P=0.07$), as 30.44% of patients had a spontaneous increase of ≥15 letters and 15.94% had a decrease of ≥15 letters.

Patients with a baseline BCVA ≥40 letters (525 eyes, 419 participants) had a statistically significant decline in 4-year BCVA averaging 10.52 letters ($P<0.001$). Fewer than 1% had a spontaneous BCVA improvement by ≥15 letters, whereas 26.67% had at least a 15-letter loss in BCVA.

Similar results emerged from analyses of change in BCVA from baseline to years 1, 2, and 3. The 4-year results held up in separate analyses of the AREDS and AREDS2 cohorts.

Analysis of GA distance from the fovea showed that GA ≤1 mm from the foveal center (552 eyes, 437 participants) was associated with a mean BCVA decline of 9.57 letters at 4 years ($P<0.001$). About 40% of patients had GA involving the foveal center at baseline. In contrast, GA lesions >1 mm from the foveal center did not change significantly over 4 years (mean change +0.18 letters). Results were consistent across all 4 years and in both AREDS studies.

By multivariate analysis, baseline BCVA and GA proximity to the foveal center had significant associations with 4-year GA growth rate ($P<0.001$).

The study results can help with patient counseling, said Rosen. Likening monthly or bi-monthly intravitreal injections to "being under house arrest" in limiting travel, he said, "you really want to be sure that you're treating the patients who really need to be treated."

Additionally, the therapy has been associated with a small risk of inflammatory response, which figures into the discussion, he added.

Before deciding whether to treat patients, Chhablani prefers to establish GA growth rate, as determined by prior imaging studies. "This study does not emphasize the progression rate, and I think that is a very important feature," he said.

Charles Bankhead is senior editor for oncology and also covers urology, dermatology, and ophthalmology. He joined MedPage Today in 2007. Follow

---

Disclosures

The study was supported by NIH, All May See Foundation, and Research To Prevent Blindness.

Del Priore reported no relevant relationships with industry. Multiple co-authors disclosed relationships with commercial interests.

Chhablani disclosed relationships with Bausch & Lomb, Genentech, and AbbVie.

Rosen disclosed relationships with Boehringer Ingelheim, Alcon Vision, Regeneron, and AbbVie.

Primary Source

Ophthalmology

Source Reference: *Shen LL, et al "Determinants of four-year visual acuity loss in geographic atrophy -- An analysis of AREDS and AREDS2" Ophthalmology 2025; DOI: 10.1016/j.ophtha.2025.01.028.*

Recommended For You

Public Health & Policy

Serious Chocolate Recall; Boy Dies in Hyperbaric Chamber; Trans Care Cancellations

Prescriptions for a Broken System

UnitedHealth CEO Andrew Witty Is Wrong. Just Plain Wrong.

Public Health & Policy

Broccoli Recall Upgraded; Some CDC Web Pages Return; Tariffs and Drug Costs

Public Health & Policy

CDC Purging Its Website After Trump Orders

Public Health & Policy

Four Medical Schools Probed by HHS; Trump's Autism Claim; Why Is the AMA Quiet?

Washington-Watch

Mass Firings at CDC, FDA Planned; Kanye West's Autism; Cooking the Perfect Egg

Medical News From Around the Web

CNN

US dodged a bird flu pandemic in 1957 thanks to eggs and luck. Can we do it again? | CNN

FORBES

Jalen Carter, Other Eagles Players Ill Before Super Bowl 2025

BECKER'S HOSPITAL REVIEW

Flu cases reach highest levels since 2009 pandemic: 6 respiratory virus updates

CLINICAL ADVISOR

Measles Outbreak Mounts Among Children in One of Texas' Least Vaccinated Counties

CANCER DISCOVERY

LINE-1 ORF1p Mimics Viral Innate Immune Evasion Mechanisms in Pancreatic Ductal Adenocarcinoma.

CIRCULATION

Ezh2 Shapes T Cell Plasticity to Drive Atherosclerosis.