PEARLS AND PITFALLS OF TREATING GA AND WET AMD

Concurrent therapy can pose clinical challenges. Here's how you can manage these patients and maximize outcomes.

By Sean D. Adrean, MD, FAAO, and Wesley Han, BS

Treatments for geographic atrophy (GA) have been shown to delay the progression of the disease, offering hope to both patients and the retina community for this previously untreatable condition. While many patients present with either GA or wet AMD, an increasing percentage of patients have both active wet AMD and GA in the same eye (Figure 1). One study of Medicare patients found that between 25.6% and 28% of GA patients have coexisting wet AMD.[1]

While the benefits of treating wet AMD are apparent in improved biomarkers and vision, the slowing of GA progression is more opaque. Treating GA is like making deposits in the bank: Over time, the savings add up, providing patients with stabilized vision for longer. Combined treatment for GA and wet AMD has the potential to preserve patients' vision longer than treating wet AMD alone (Figure 2). However, with the advent of new and better treatment options for both conditions, clinicians must be aware of various treatment pitfalls to ensure the best outcomes for patients.

CLINICAL AND RETROSPECTIVE TRIAL DATA

With the completion of the OAKS and DERBY trials for pegcetacoplan (Syfovre, Apellis) and the GATHER trials for avacincaptad pegol (Izervay, Astellas), the FDA approved these therapies in February and August 2023, respectively. While all three studies excluded patients with prior choroidal neovascularization (CNV) in the study eye, OAKS and DERBY continued patients who developed CNV in the study eye, beginning anti-VEGF treatment at the investigator's discretion. GATHER2 discontinued these patients.

The 2-year outcomes of OAKS and DERBY showed a reduction of GA progression of 19% and 22% in the every-month (EM) groups and 16% and 18% in the every-other-month (EOM) groups, respectively.[2] In the 3-year GALE extension study of pegcetacoplan, treated eyes experienced a 42% and 28% reduction when receiving EM and EOM injections, respectively, and GA progression was delayed by 1.5 years after 5 years of treatment.[3,4]

The 2-year GATHER2 results for avacincaptad pegol demonstrated 14% and 19% reductions in GA progression for EM and EOM injections, respectively.[5] The open-label GATHER2 extension demonstrated a 37% to 40.5% reduction after 3.5 years of treatment.[6]

KEY TAKEAWAYS

- Combined treatment for geographic atrophy (GA) and wet AMD can preserve patients' vision longer than treating wet AMD alone.
- The authors' research shows a 44% reduction in the rate of GA progression following GA treatment initiation in combination with anti-VEGF therapy compared with the prior year of patients only receiving anti-VEGF treatments.
- When treating concurrent GA and wet AMD, clinicians can schedule follow-up treatments based on the treatment the patient received that day.
- To avoid increased injection volume after two injections within a short time, consider treating wet AMD and GA on different days.

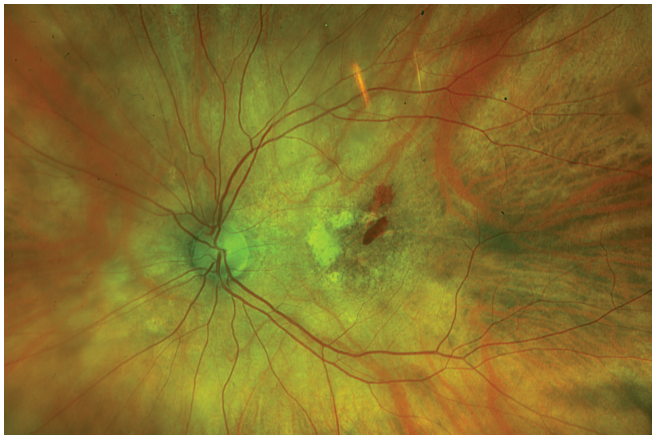

Figure 1. This patient with both CNV due to wet AMD and GA may benefit from combined treatment of both conditions.

OAKS and DERBY reported that 12.2% and 6.7% of GA patients developed CNV when receiving EM and EOM treatments (sham was 3.1%), while at 2 years, GATHER2 reported 11.6% CNV occurrence (sham was 9.0%).[2,5]

In GALE, patients who developed wet AMD lost an average of 2.8 letters at wet AMD diagnosis compared with the prior visit and lost 4.3 letters by month 12 compared with their visit when wet AMD was diagnosed.[3]

Yet there remains sparse research on patients with pre-existing wet AMD with coexisting GA. Thus, we recently identified and examined 31 patients with pre-existing wet AMD who also had nonfoveal GA develop during their wet AMD treatment. We retrospectively analyzed the data of patients who were previously treated for wet AMD for at least 1 year before beginning pegcetacoplan treatment and continuing both pegcetacoplan and anti-VEGF treatments for another year. We excluded wet AMD patients with subfoveal GA and/or macular atrophy, as that constitutes a distinct disease state with poor visual prognosis with anti-VEGF treatment.[7,8]

The 1-year outcomes showed a 44% reduction in the rate of GA progression following pegcetacoplan treatment initiation in combination with anti-VEGF therapy compared with the prior year when patients were only receiving anti-VEGF treatments.[9] The average vision changed from 68.3 ETDRS letters to 67.9, which was nonsignificant, and 22 patients remained dry while nine had persistent but non-worsening retinal fluid.[9]

Patients were previously treated for wet AMD on average for 6.5 years, using a treat-extend-stop protocol.[9] After 1 year of receiving both treatments, the average anti-VEGF injection interval was 12 weeks while pegcetacoplan treatments averaged every 8.1 weeks.[9,10]

Pearls for Treating GA and CNV

- Treat both GA and wet AMD (should have one visit per disease process)
- Monitor wet AMD between injections
- Schedule follow-up based on the eye treated and disease state
- Prioritize wet AMD in treatment

Pitfalls of Concurrent Treatment

- More complex workflow, charting, and scheduling
- Injection fatigue
- Missed visits or worsening of CNV during GA treatment visits
- Billing issues

CONSIDERATIONS FOR MANAGING GA AND CNV

With treatment options for both GA and wet AMD, we can reduce exudation from CNV to restore lost vision, and slow GA lesion growth to preserve vision longer. Despite these treatments, some clinicians hesitate to treat both diseases when they present concurrently, mainly due to a dearth of research regarding these coexisting disease states.

Clinical Practice Pearls

From personal clinical experience, we learned that for patients with bilateral GA, it helps to treat both eyes on the same day and keep the same time interval between treatments. We currently treat most GA patients at a 5- to 6-week time interval. Yet, unlike patients in the OAKS/DERBY/GALE trials, we do not treat both wet AMD and GA on the same day in the same eye. This helps avoid increased injection volume after two injections within a short time. In the trials, clinicians waited 30 minutes between treatments, which is not practical for real-world clinics because it increases visit time and inhibits clinic flow.

In our clinic, we schedule follow-up based on the treatment the patient received that day. If a patient presents for GA treatment in the left eye, we schedule the follow-up visit only for the GA treatment. We still review the chart to make sure the wet AMD treatments have been scheduled, and all staff involved carefully review the chart and confirm with the patient the correct treatment for the correct eye. This treatment approach can be particularly challenging when a patient is receiving four shots total (two per eye) at varying treatment intervals. While injections for CNV vary based on disease activity, patients typically have fixed intervals for GA therapy.

Overcoming Injection Fatigue

Another important pitfall to avoid is injection fatigue. At the onset, we iterate that GA therapy requires a lifelong commitment to experience the benefits, and we often act as cheerleaders, advocating for the patient to continue treatment. During visits for GA, we discuss how the treatment is slowing the disease process, educate patients on the characteristics of progression using autofluorescence,

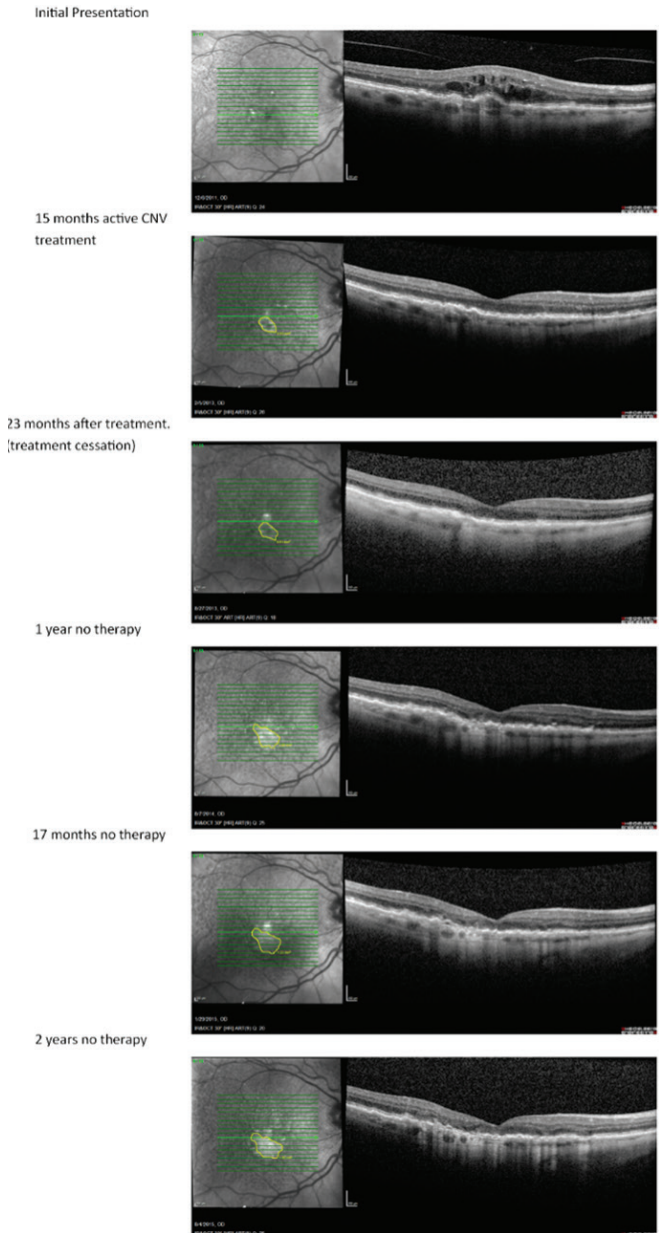

Image courtesy: This figure has been submitted to Retina but has yet to be accepted for publication

Figure 2. This patient with CNV reached treatment cessation but developed GA.

and describe how GA encroaches on central vision. During visits for wet AMD, we spend more time reviewing the OCT images with the patient and (hopefully) highlighting the regression in exudation and improved vision.

Given the number of injections required, patients may also miss their appointments for various reasons. Because it becomes harder to track wet AMD visits when patients are also receiving GA treatments (ie, with more visits, patients are more likely to forget a visit or be confused), patients may fall through the cracks. When assessing risk to vision, we must be preferential toward wet AMD treatments and be ready to postpone the GA treatment if the wet AMD worsens. It is much more difficult to recover vision after multiple fluid recurrences from CNV. Slowing GA is important, but anticomplement therapy does not restore vision.

Patients with GA may at times complain of vision loss, which is typical. When this occurs, we mention that patients with GA often have fluctuating vision depending on the day or week. We review their chart and highlight their current vision and range of vision over several visits to encourage them to continue with the treatment regimen.

BALANCING A BUSY SCHEDULE

Patients with wet AMD and GA may be successfully treated for both conditions, and our study found an associated reduction in GA with maintained vision.[9] However, complex workflows, the management of multiple treatments (sometimes in both eyes), and patient charting require greater vigilance from clinicians and staff. To ensure successful outcomes, treatment of both diseases requires proactive scheduling, close monitoring of both diseases, and efficient communication to ensure patients do not fall through the cracks. Our ability to further protect the vision of patients with coexisting wet AMD and GA represents an important paradigm shift for this subset of patients. ■

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