Recalcitrant Neovascular Macular Degeneration After Anti-VEGF Therapy: An Ongoing Challenge

Despite the remarkable success of anti-VEGF therapy in halting visual loss in eyes with neovascular macular degeneration, one major challenge for the retinal clinician remains the management of eyes that demonstrate signs of persistent exudation (ie, macular edema, subretinal fluid, or retinal pigment epithelial detachment) after anti-VEGF treatment. There is general agreement that improved visual acuity is associated with reduction of exudation and normalization of retinal anatomy on optical coherence tomography (OCT).

The management of eyes with persistent exudation, sometimes even after intensive anti-VEGF therapy, remains a major therapeutic challenge. The options available to clinicians include switching anti-VEGF agents, perhaps using an agent with a higher binding affinity to VEGF, decreasing the re-treatment interval from 4 to 2 weeks (which has been described for bevacizumab), or using a higher-dose anti-VEGF agent.

In this issue of OSLI Retina, Wykoff and colleagues report success using high-dose ranibizumab in treating recalcitrant neovascular macular degeneration. They used 2-mg doses of ranibizumab (four times the commercially available dose) in eyes with persistent exudation after prior monthly treatment with normal-dose ranibizumab. In an earlier paper, these authors demonstrated that use of high-dose ranibizumab in these eyes was associated with improved vision after three monthly doses of drug. In the current study, they followed these eyes for another 12 months, using a 4- or 6-week capped PRN treatment approach. Not surprisingly, most eyes required treatment at every PRN interval; clearly, these were eyes with highly active disease. An important observation was that the visual acuity results were the same at both 4- and 6-week PRN dosing intervals, suggesting that such less intensive therapy with high-dose ranibizumab can preserve vision. Interestingly, the anatomic results, as demonstrated by OCT, were better in the 4-week compared to the 6-week group.

One major frustration for retinal clinicians is that there is no demonstrated way of predicting which eyes with wet age-related macular degeneration (AMD) will require such intensive therapy. No systemic biomarker has yet been identified, and the preoperative anatomic characteristics on OCT are also nonpredictive. We do not have a biologic or physiological understanding of why some eyes require intense therapy to maintain normal anatomy. Basic investigations of the biology of wet AMD are vital to advancing clinical therapy of this disorder. In addition, it is clear that there is a need for additional therapeutic agents that attack the abnormalities of wet AMD using different molecular targets as well as novel delivery systems that can help mitigate the treatment burden of this devastating chronic disease.

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ABSTRACT: This editorial describes the challenge of managing eyes that demonstrate signs of persistent exudation after anti-VEGF treatment and illuminates the significance of a new report of using high-dose ranibizumab in treating recalcitrant neovascular age-related macular degeneration.

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