

# Nonselective Followed by Selective VEGF Blockade May Benefit AMD Patients

Combining nonselective and selective VEGF blockade may provide clinical benefit in the treatment of neovascular age-related macular degeneration.

REVIEWED BY MARK S. HUGHES, MD

**N**onselective vascular endothelial growth factor (VEGF) blockade using bevacizumab (Avastin; Genentech, San Francisco) induction and selective VEGF<sub>165</sub> blockade with pegaptanib (Macugen; OSI/Eyetech and Pfizer, New York, NY) as maintenance therapy may offer clinically meaningful outcomes with acceptable safety profiles in patients with age-related macular degeneration (AMD).

According to Mark S. Hughes, MD, and Delia N. Sang, MD, reporting in *Ophthalmic Surgery, Lasers & Imaging*,<sup>1</sup> an extensive body of research has established VEGF-A as both necessary and sufficient in promoting ocular neovascularization and as the most potent known promoter of vascular permeability. The use of bevacizumab for induction of regression of choroidal neovascularization in macular degeneration followed by the use of pegaptanib for maintenance of regression was studied.

## SEQUENTIAL, COMBINATION THERAPY

“As the pharmacotherapy of AMD evolves, it is likely that, as is true in oncology, different therapeutic agents will be employed sequentially and in combination as improvements in patient outcomes are sought to maximize benefits while minimizing risks,” the authors wrote. Although there have been no clinical trials, bevacizumab, a pan-VEGF blockade agent, has been extensively used as an off-label in the treatment of CNV. The benefits, including rapid response are widely accepted, but with limited data on either short-term or long-term risks. Pegaptanib, a selective-VEGF blockade drug, in contrast, does not demonstrate a rapid response, but its

low intraocular and systemic risks are well documented. In addition, “pegaptanib has proven clinically effective as a treatment for all forms of neovascular AMD,” said Dr. Hughes, from the Schepens Eye Research Institute and the Department of Ophthalmology, Harvard Medical School.

“Pegaptanib has proven clinically effective as a treatment for all forms of neovascular AMD.”

The investigators treated 20 treatment-naïve patients with all angiographic subtypes of choroidal neovascularization secondary to AMD with intravitreal bevacizumab. Patients had a broad range of baseline vision. Included patients received one injection of bevacizumab 1.25 mg followed by a series of nine intravitreal injections of pegaptanib 0.3 mg given at 6-week intervals during 54 weeks. Pegaptanib therapy was initiated 3 weeks following bevacizumab induction. “Additional injections of bevacizumab could be administered if there was at least a 15% increase in the greatest linear dimension of the neovascular lesion as evaluation by fluorescein angiography at weeks 18, 24, 36, and 54,” Dr. Hughes wrote.

Patients were monitored using Snellen charts, slit-lamp biomicroscopy, and dilated funduscopy at baseline and at weeks 3, 9, 15, 18, 21, 24, 27, 33, 36, 39, 45, 51, and 54. The investigators also performed fluorescein

## Earn Free Online CME Credits!

- Obtain online CME credits on your schedule, anytime and anywhere
- Online instructions and support help you get started
- Instant, real-time grading with printable certificate
- Track your online credits

### Featured CME Course:

- **Update on Pharmacologic Treatment of Diabetic Macular Edema**
- **Molecular Biology Of Diabetic Retinopathy**
- **Hyperglycemia and Microvascular Complications**

**Tomorrow's CME is here Today —and it's FREE**

www.CMEToday.net

## MACULA

angiography and optical coherence tomography at baseline and weeks 18, 24, 36, and 54.

### IMPROVEMENT IN MEAN VISUAL ACUITY

There was an improvement in mean visual acuity from approximately 20/200 at baseline to 20/80, with 1 year follow-up, the authors wrote. An improvement in retinal thickness, from -47  $\mu\text{m}$  to -297  $\mu\text{m}$  was seen in all patients. "Adverse events were limited to transient irritation or redness," they reported. "No significant elevation in intraocular pressure occurred following either bevacizumab or pegaptanib injections."

Bevacizumab should be approached with caution, as it has not been evaluated in long-term randomized controlled trials of patients with ocular neovascular disease.

Drs. Hughes and Sang wrote that intravitreal bevacizumab has not been evaluated in long-term, randomized, controlled trials of patients with ocular neovascular disease. Therefore, this agent for the treatment of AMD should be approached with caution, and its use is minimized in this treatment approach. In addition, pegaptanib was effective in maintenance of the improvement and its long-term safety has been established. Although this is a small case series, these results are comparable to those seen in the MARINA and ANCHOR trials, but with the initial response to therapy attributed to bevacizumab and the plateau in response maintained with pegaptanib.

"Evidence indicates that VEGF<sub>165</sub> is the isoform primarily responsible for pathological ocular neovascularization," the authors wrote. "Despite the inherent limitation of small case series, the results of treatment with this combination of selective and nonselective VEGF blockade applied in an induction-maintenance paradigm are encouraging." ■

*Mark S. Hughes, MD, and Delia N. Sang, MD, are from the Schepens Eye Research Institute and the Department of Ophthalmology, Harvard Medical School. Drs. Hughes and Sang receive research funds from OSI/Eyetech. Dr. Hughes may be reached at Ophthalmic Consultants of Boston, 50 Staniford St., Ste 600, Boston, MA 02114.*

1. Hughes MS, Sang DN. Safety and efficacy of intravitreal bevacizumab followed by pegaptanib maintenance as a treatment regimen for age-related macular degeneration. *Ophthalmic Surg Lasers Imaging*. 2006;37:446-454.