

# Macugen Improved Vision, Reduced Macular Thickness

Patients who received the drug improved their vision by one, two or three lines compared with those who received the standard of care.

BY LAURA SUAREZ, ASSOCIATE EDITOR

**P**egaptanib sodium injection, a treatment approved for the treatment of neovascular age-related macular degeneration, may also be beneficial in patients with diabetic macular edema (DME).

Investigators evaluated the Food and Drug Administration-approved dosing of pegaptanib sodium injection (Macugen, Eyetech Pharmaceuticals, Inc) – 0.3 mg once every 6 weeks – in DME patients. Although Macugen is not yet indicated for the treatment of DME, clinical trials have shown that it was well tolerated and effective in patients with the condition. Lawrence J. Singerman, MD, FACS, clinical professor of ophthalmology at the Case Western Reserve University School of Medicine, presented findings at the Association for Research in Vision and Ophthalmology (ARVO) 2005: Global Networking. Macugen is a pegylated anti-vascular endothelial growth factor (anti-VEGF) aptamer that binds to VEGF to combat increased permeability and angiogenesis.

## RANDOMIZED TO MACUGEN OR PLACEBO

A total of 172 patients from 38 centers in the United States, Canada, Australia and Europe were enrolled in the exploratory, phase 2 clinical trial. Patients had clinically significant macular edema (CSME) and a visual acuity between 20/50 and 20/320. They were randomized to 0.3 mg, 1 mg, 3 mg of Macugen or placebo once every 6 weeks for 12 weeks. After week 12, the treating ophthalmologist determined if additional injections were necessary, Dr. Singerman said. The study was followed through until week 36, when retinal thickness, visual acuity and the need for either focal or grid laser therapy were the clinical endpoints.

Anti-VEGF drugs may present an opportunity to reverse the trend of diabetic retinopathy.

All doses of Macugen were well tolerated by patients, and the lowest dose provided patients with better visual acuity and a greater reduction in central retina thickness compared with placebo. It also lessened the patients' need for laser therapy. "Three-tenths milligrams is the dose [of Macugen] that was approved for use in age-related macular degeneration and likely will be the dose used in diabetic retinopathy," Dr. Singerman said during the presentation. Results from the clinical trial are based on the 0.3-mg dose.

A statistically significant number of patients in the Macugen group experienced zero or more, one or more or two or more lines of vision gained in their eyes compared with patients in the placebo group, and it continued for three or more lines gained. Dr. Singerman said this was the key finding of the study. "This exploratory study was not powered or designed to show effects on vision, so the statistically significant effects are all the more compelling," he said.

The retinopathy severity score, according to criteria from the Wisconsin Reading Center, improved by two steps in 13% of patients who took Macugen compared to 3% of placebo patients. A one-step progression was seen in 28% of Macugen patients versus 13% of placebo patients. "This is preliminary data," Dr. Singerman said. "But to me, this is very encouraging." Visual acuity was

also better in this group compared to the placebo group ( $P=.042$ ).

### DECREASE IN RETINAL THICKNESS

Central macular retinal thickness also decreased significantly by a mean of -68 microns in patients assigned to the Macugen group. Patients assigned placebo had a mean increase of central macular retinal thickness of 3.7 micron ( $P=.021$ ). Dr. Singerman said that 49% of patients who took Macugen experienced a decrease of  $\geq 75$

microns in retinal thickness and 42% of patients experienced a decrease in thickness that was  $\geq 100$  microns. Only 19% and 16% of placebo patients, respectively, experienced these decreases.

Serious adverse events were balanced between the Macugen and placebo groups. In 5% of Macugen patients and 7% of placebo patients, vitreous hemorrhage occurred. One out of 652 Macugen injections produced endophthalmitis; however, no severe vision loss resulted from the complication.

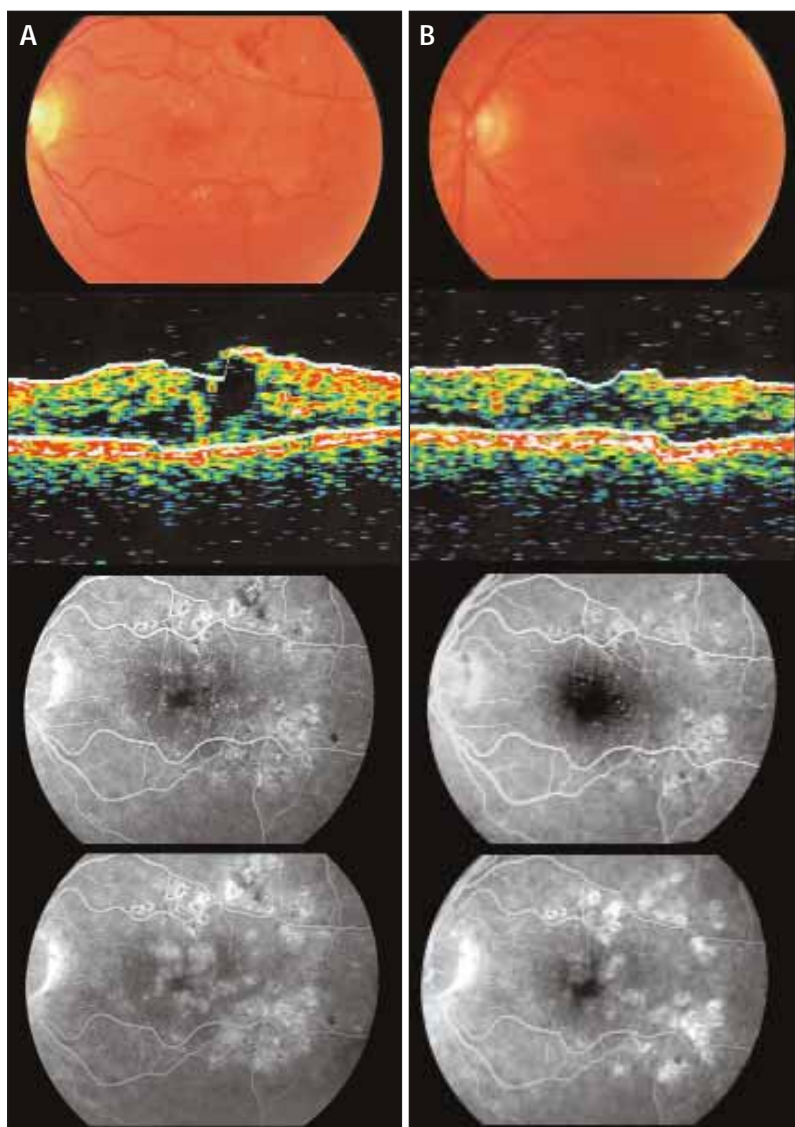


Figure 1. Color pictures of optical coherence tomography (OCT) and fluorescein angiography, showing changes from baseline (A) to the week 36 follow-up visit (B) in a patient treated with Macugen for CSME. The color pictures and the angiograms show improvement in the macular edema, and OCT shows reduction in ocular thickness. Visual acuity also improved from 20/50 at baseline to 20/25 at week 36.

### DOES NOT CAUSE CATARACTS

"Macugen is well tolerated by the [diabetic] eye," Dr. Singerman said. "It doesn't cause cataracts or accelerate them. There is no chronic increase in intraocular pressure, and endophthalmitis appears to be a risk factor modifiable by good sterile technique."

Macugen, in the dosing of 0.3 mg once every 6 weeks, allowed for improved or stabilized vision in patients with DME, and the effects were statistically significant for up to three lines of improvement, Dr. Singerman said. A phase 3 clinical trial will begin shortly. Other results will be presented at the upcoming American Academy of Ophthalmology meeting, held October 15 to 18, in Chicago, he said.

"It really is very encouraging what these data are suggesting because of what we understand of VEGF's role in diabetic retinopathy. By providing an anti-VEGF drug, we may be able to reverse some of these changes in diabetic retinopathy." ■

*Lawrence J. Singerman, MD, FACS, is a clinical professor of ophthalmology at the Case Western Reserve University School of Medicine and practices at the Retina Associates of Cleveland, Ohio. He has a financial interest with Eye Tech, and he can be reached at (216) 831-5700 or [lsingerman@retina-assoc.com](mailto:lsingerman@retina-assoc.com).*

Singerman LJ. Findings of the phase 2 trial of the safety and efficacy of pegaptanib sodium (Macugen) in patients with diabetic macular edema. Presented at ARVO 2005: Global Networking. May 1-5, 2005. Ft Lauderdale, Fla.