

Pegaptanib Shows Promise for Macular Edema Associated With CRVO

Selective VEGF₁₆₅ inhibition is theoretically attractive in CRVO.

BY CONNI BERGMANN KOURY, EDITOR-IN-CHIEF

In a randomized, controlled clinical trial of patients with macular edema secondary to central retinal vein occlusion (CRVO), treatment with pegaptanib injections (Macugen; OSI/Eyetech, Pfizer, New York, NY) was associated with better visual acuity compared with a sham injection.

"Further studies are needed to confirm selective [vascular endothelial growth factor] VEGF blockade as an efficacious and safe therapy for patients with this unmet condition," said John A. Wells III, MD, from the Palmetto Retina Center in Columbia, SC. Dr. Wells presented results from the exploratory phase 2 clinical trial at the Cannes Retina Festival 24th Annual Meeting of the American Society of Retinal Specialists (ASRS) & 6th Annual Meeting of the European Vitreoretinal Society (EVRS).

Central retinal vein occlusion is the second leading cause of vision loss due to retinal vascular disease. Characterized by increased retinal venous pressure, diffuse intraretinal hemorrhages and optic disc edema, the main cause of vision loss is cystoid macular edema (CME). Despite the 130,000 new cases of CRVO that occur each year, there is no proven treatment for this condition.

VEGF ROLE WELL ESTABLISHED

The role of VEGF to increase vascular permeability is

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well known, Dr. Wells said. "Pegaptanib has been shown to slow vision loss in neovascular age-related macular degeneration and reduce diabetic macular edema, so it makes sense to test it in CRVO where VEGF overexpression is present."

There is a paradox of VEGF, however, in that it has both positive and negative effects, Dr. Wells said. "Certainly in CRVO, where there is damage to the retinal vasculature, ischemia and damage to the neurosensory retina, selective VEGF blockade may be especially important. Nonselective VEGF inhibition may exacerbate retinal tissue damage. Therefore, selective VEGF₁₆₅ inhibition is theoretically attractive in CRVO," (Figure 1).

STUDY PARAMETERS

The purpose of this study was to explore the safety and efficacy of pegaptanib when given by intravitreal injection every 6 weeks in patients with recent vision loss due to macular edema secondary to CRVO. In this

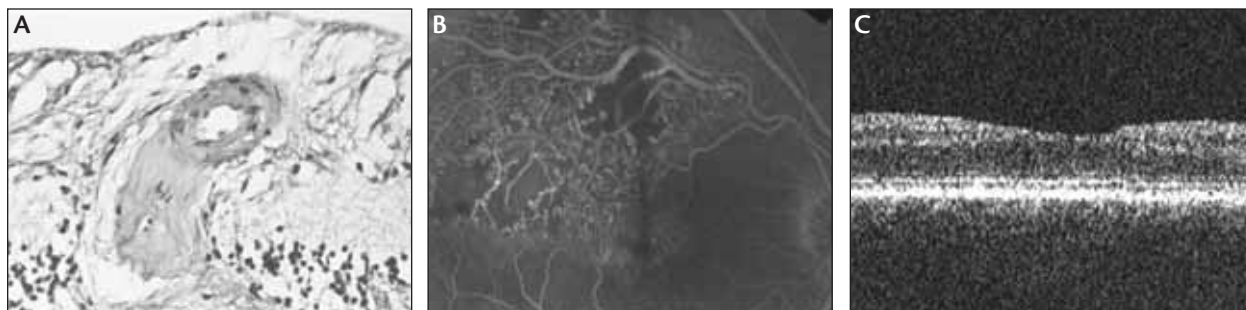


Figure 1. Selective VEGF blockade may be especially important in retinal vascular diseases: Damage to retinal vasculature (A); vascular occlusion and hyperpermeability (B); and damage to neurosensory retina (C).

dose-ranging, sham-controlled, randomized, multicenter trial, patients were stratified by study center and baseline visual acuity (≤ 34 letters vs > 34 letters, or approximately 20/200 Snellen equivalent). The patients were randomized to pegaptanib injection 0.3 mg, 1 mg or sham. Panretinal photocoagulation was permitted for neovascularization according to the Central Vein Occlusion Study protocol.

To be included in the study, patients had to have CRVO within 6 months prior to baseline, BCVA in the study eye between 65 and 20 Early Treatment of Diabetic Retinopathy Study (ETDRS) letters inclusive (ie, 20/50 to 20/400 Snellen equivalent), and have macular edema as determined by ocular coherence tomography with central retinal thickness $\geq 250 \mu\text{m}$ at baseline and day 0.

Patients received an injection every 6 weeks for 24 weeks for a total of five injections; results were analyzed at 30 weeks. Baseline vision was well balanced among the groups, with a mean visual acuity in the study eye of 50.4 letters (about 20/100 Snellen equivalent).

RESULTS

“There was an early and sustained treatment effect with pegaptanib in both doses compared to sham,” Dr. Wells said. At 30 weeks patients assigned to the 0.3-mg and 1-mg doses showed a gain of seven and 10 letters respectively versus a loss of three letters in the sham group. This means that on average the 1-mg dose group gained almost three lines (13 letters) compared with sham, and the 0.3-mg dose gained two lines (10 letters) compared with sham. The difference between the 1-mg group and sham, but not the 0.3-mg group and sham, was statistically significant (Figure 2).

Additionally, 6% and 9% of patients in the 1-mg and 0.3-mg dose groups lost fewer than three lines of vision compared with 31% of the sham group at week 30. This difference was statistically significant (Figures 3 and 4). Thirty-nine percent and 36% of the 1-mg and 0.3-mg

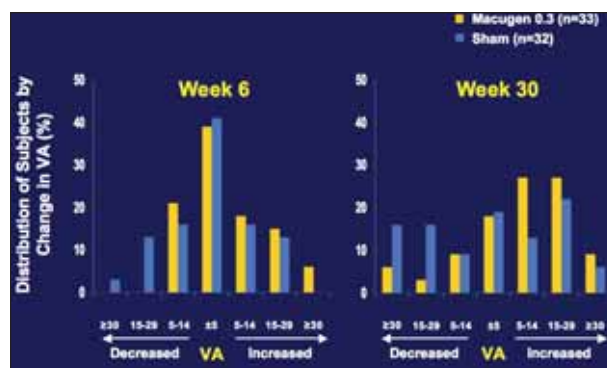


Figure 2. Distribution of patients by change in visual acuity over time shows pegaptanib 0.3-mg patients shifting to the left towards better visual acuity in comparison to sham patients.

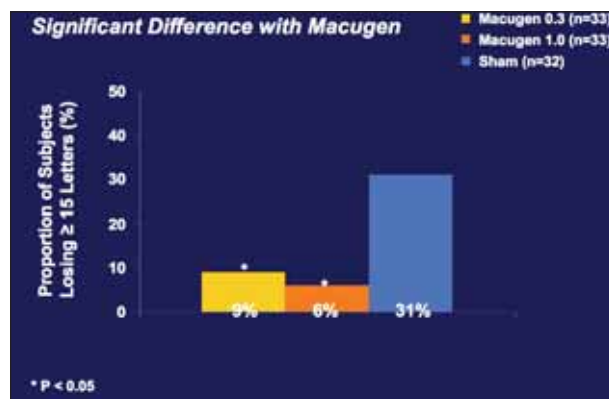


Figure 3. There was a significant difference in the proportion of patients losing fewer than three lines of visual acuity favoring the pegaptanib groups.

dose, respectively, gained three lines of vision versus 28% of the sham. Though not significantly different, this result highlights the often good natural course of untreated CRVO, emphasizing the need for randomized clinical trials in this condition.

All groups showed an early and sustained decline in OCT-measured central retinal thickness, with the 1-mg

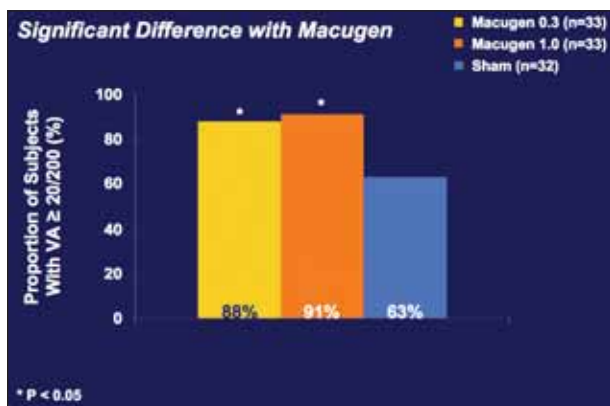


Figure 4. There were significantly more patients with visual acuity \geq 20/200 at week 30.

dose declining 186 μ m, the 0.3-mg dose declining 253 μ m and the sham group declining 151 μ m. While not statistically significant, there was a trend toward a greater reduction in macular edema in the treatment arms.

There were no serious ocular or systemic adverse events; one patient in the sham group discontinued the study due to vision loss of more than three lines.

COMMENTS

"Patients receiving pegaptanib showed better visual acuity and anatomical results than patients receiving sham with a favorable safety profile," Dr. Wells concluded. "Given the suggested deleterious effects of nonselective VEGF blockage in ischemic retina, selective blockage may have a significant role in CRVO."

In an interview with *RETINA TODAY*, Dr. Wells said that the pegaptanib data for CRVO looks very positive from his personal experience. "I hope that we get the chance to do longer follow-up on these patients, because I think it's going to be important to see what happens after you stop treatment. There are a lot of unknowns with regard to the long-term course," he said.

"To date this is the first ever randomized clinical trial that has shown a treatment benefit in CRVO, so this is a very important step," Dr. Wells said. ■

John A. Wells III, MD, is in private practice at the Palmetto Retina Center and is assistant clinical professor of ophthalmology at the University of South Carolina School of Medicine. Dr. Wells is a consultant for and receives travel fees from OSI/Eyeteck and Pfizer. He may be reached at jackwells@palmettoretina.com or 803-931-0077.

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