

Ranibizumab Slows Macular Vision Loss

REVIEWED BY QUAN DONG NGUYEN, MD, MSc, AND PETER A. CAMPOCHIARO, MD

Ranibizumab (Lucentis; Genentech, San Francisco), which is the first treatment to cause significant improvement in vision in 35% to 40% of patients with neovascular age-related macular degeneration (AMD), has recently also shown promise in the treatment of diabetic macular edema (DME).

According to a news release from Johns Hopkins Wilmer Eye Institute, researchers were encouraged by the effect of ranibizumab in people with DME. Quan Dong Nguyen, MD, MSc, an assistant professor of ophthalmology at the Wilmer Eye Institute at Johns Hopkins and colleagues injected the drug into the eyes of 10 people losing their sight from macular edema, one of many complications of diabetes.

Over the course of several months of therapy, patients in the preliminary study could read an average of two more lines on the standard eye chart, according to the report in the *American Journal of Ophthalmology*.¹ Macular thickness in these patients decreased an average of 85%.

LONGER TRIAL ON THE WAY

“The results are impressive, although we will not know until we begin a larger clinical trial what the long-term benefits of the drug might be,” said Dr. Nguyen. The Hopkins group believes that ranibizumab interferes with vascular endothelial growth factor (VEGF), which is released when the oxygen supply in the eye is restricted by blood vessel damage related to diabetes. VEGF causes blood vessels to become leaky resulting in collection of fluid in the macula.

“We’ve suspected for awhile that ranibizumab’s ability to shut down VEGF’s signaling would do the trick because it’s highly likely that VEGF is the culprit when it comes to diabetic macular edema [DME],” said Dr. Nguyen. More than 4 million patients with diabetes in the United States have diabetic retinopathy and, according to the National Eye Institute, one in 12 of those experiences at least some vision loss.

All 10 patients in the study had some vision loss at the start of the clinical trial. Ranibizumab was administered at 1, 2, 4, and 6 months. Macular thickness was measured at each point in the study using optical coherence tomography. “Within a week, several patients experienced dramatic reductions in the thickness of their maculas, and there were

further improvements with each injection,” said Peter Campochiaro, MD, the Dolores and George Eccles Professor of Ophthalmology and Neuroscience at The Johns Hopkins University School of Medicine, senior author of the study.

Mean values at baseline were 503 μm for foveal thickness, 9.22 mm^3 for macular volume, and 28.1 letters (20/80) read on an Early Treatment Diabetic Retinopathy Study (ETDRS) visual acuity chart, the investigators wrote. At 7 months, 1 month after the fifth injection, the mean foveal thickness was 257 μm —a reduction of 246 μm (85% of the excess foveal thickness present at baseline; $P=.005$ by Wilcoxon signed-rank test for likelihood that this change is due to ranibizumab rather than chance).

Dr. Nguyen and colleagues wrote that the macular volume was 7.47 mm^3 , representing a reduction of 1.753 (77% of the excess macular volume at baseline; $P=.009$). “Mean visual acuity was 40.4 letters (20/40) which was an improvement of 12.3 letters ($P=.005$).

No ocular or systemic adverse events were noted and the injections were well tolerated.

RESEARCH INDICATES VEGF ROLE IN DME

The investigators wrote that previous studies have also suggested that VEGF may play a role in DME. “An orally administered kinase inhibitor that blocks VEGF receptor signaling caused a dose-dependent reduction in foveal thickness in patients with DME.”

According to Dr. Nguyen and colleagues, “The most important question raised by this study is whether intraocular ranibizumab can provide long-term benefit in patients with DME. The mean improvement of 12.3 letters of visual acuity over 7 months is suggestive, but a larger double-masked, randomized, controlled trial that will span several years is needed to determine the ultimate value of ranibizumab for patients with DME. Such a trial is being planned.”

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1. Nguyen QD, Tattipnar S, Shah SM, et al. Vascular endothelial growth factor is a critical stimulus for diabetic macular edema. *Am J Ophthalmol*. 2006;142:961-969.