Using Aflibercept to Treat Diabetic Macular Edema

Drug shown to be safe and effective in VIVID and VISTA trials.

BY DIANA V. DO, MD

Untreated diabetic macular edema (DME) can lead to vision loss in patients with diabetic retinopathy. Current treatment options for DME include intravitreal anti-VEGF agents (ranibizumab [Lucentis, Genentech] and bevacizumab [Avastin, Genentech]), laser photocoagulation, intravitreal steroids or steroid delivery devices, or vitrectomy in select cases.

This article reviews the results of the VIVID and VISTA trials, which were designed to investigate the effects of intravitreal aflibercept (Eylea, Regeneron) in eyes with center-involved DME. In these studies, intravitreal aflibercept was shown to be superior to laser photocoagulation for treating center-involved DME and appeared to be safe in patients with diabetic retinopathy. The following information was presented publicly at Retina Subspecialty Day at the Annual Meeting of the American Academy of Ophthalmology in 2013[1] and at the Angiogenesis, Exudation, and Degeneration meeting in 2014.

VIVID AND VISTA

The VIVID and VISTA studies were parallel, phase 3, randomized clinical trials conducted in more than 120 centers around the world. The primary outcome of the studies was mean change in best corrected visual acuity (BCVA) at 1 year. The VIVID trial was conducted in Europe and in other countries outside of the United States, and the VISTA trial was conducted in the United States.

Eyes with center-involved DME as determined with spectral-domain optical coherence tomography (OCT) were randomized to 1 of 3 treatment groups: (a) 2.0 mg aflibercept every 4 weeks, (b) 2.0 mg aflibercept every 8 weeks after 5 scheduled monthly injections, and (c) laser photocoagulation. Eyes assigned to the aflibercept treatment groups were given sham laser treatments; eyes assigned to the laser treatment group were given sham injections.

> Patients in the aflibercept treatment groups had a greater mean reduction in central retinal thickness compared with patients in the laser treatment group.

Approximately 85% to 94% of patients completed the primary outcome of the study. The mean age of enrollment was 64 years. Mean hemoglobin HbA1c at baseline was approximately 8%. The mean baseline score on the diabetic retinopathy severity scale (DRSS) was 43 to 53, which corresponds with severe nonproliferative diabetic retinopathy.

RESULTS

Patients in either aflibercept treatment group had BCVA outcomes superior to those in the laser group. Patients treated with aflibercept gained a mean +10.5 to +12.5 letters; patients treated with laser gained a mean +1.0 letter.

In the aflibercept treatment groups, 55% to 65% of eyes gained 10 or more letters and 31% to 43% of eyes gained 15 or more letters.

Patients in the aflibercept treatment groups had a greater mean reduction in central retinal thickness compared with patients in the laser treatment group. At 1 year, eyes treated with aflibercept had a mean reduction of 183 µm to 195 µm in OCT retinal thickness compared with a reduction of 66 µm to 73 µm in laser-treated eyes. Small fluctuations were seen in central subfield thickness in the aflibercept treatment group receiving injections every 8 weeks. However, these fluctuations were less than 30 µm and had no effect on BCVA outcomes at 1 year.

Patients who were randomized to the aflibercept treatment groups had a greater mean reduction in their DRSS scores than patients randomized to the laser treatment group. Approximately 28% to 33% of aflibercept treated eyes had a 2-step or greater improvement in DRSS scores compared with 7% to 14% of laser-treated eyes.

SAFETY

Within both VIVID and VISTA, the occurrence of serious systemic adverse events was about equal between the aflibercept treatment groups and the laser treatment group. The aflibercept treatment groups and the laser treatment group showed similar rates of atherothrombotic events.

There were no safety signals associated with aflibercept use. In addition, there was a very low rate of intraocular inflammation in patients randomized to the aflibercept treatment groups.

THE FUTURE

These results are promising and show that treating DME with intravitreal aflibercept is an effective method for achieving BCVA results that are superior to laser photocoagulation. The very low number of serious systemic adverse events at 1 year also suggests that aflibercept is safe. These data confirm that intravitreal anti-VEGF therapy is the best treatment for center-involved DME and that aflibercept may be an effective and safe option for patients with DME. ■

Diana V. Do, MD, is Vice Chair for Education, Director of the Carl Camras Center for Innovative Clinical Research in Ophthalmology, and Director of the Ophthalmology Residency Training Program at the Truhlsen Eye Institute, University of Nebraska Medical Center. Dr. Do has received research funding from Regeneron and Genentech. She also serves as a consultant for both Regeneron and Genentech. She may be reached at Diana.Do@unmc.edu.

1. Do DV. Intravitreal aflibercept injection (IAI) for diabetic macular edema (DME): 12-month results of VISTA-DME and VIVID-DME. Paper presented at: the 2013 Annual Meeting of the American Academy of Ophthalmology; November 16-19, 2013; New Orleans, LA..