My Use of Aflibercept in Clinical Practice

BY PHILIP J. ROSENFELD, MD, PHD

In November, the US Food and Drug Administration granted approval for aflibercept (Eylea, Regeneron) for use in the treatment of wet age-related macular degeneration (AMD).[1] This decision was largely based on the 1-year data obtained in the VIEW 1 and VIEW 2 studies, which showed that aflibercept injected every 8 weeks was clinically equivalent to Lucentis (ranibizumab, Genentech) injected every 4 weeks for maintaining visual acuity (less than 15 letters of vision loss) over 52 weeks.[2,3] This decrease in frequency of dosing is obviously desirable.

The 2-year data from these studies, released 1 week after FDA approval was received, tell a somewhat different story, but still show promise for aflibercept. The data show that over the course of the second year, patients in the aflibercept group required an average of 0.5 fewer injections than patients in the ranibizumab group (4.2 vs 4.7), while achieving very similar results in visual acuity (7.9 letter gain for ranibizumab vs 7.6 letters for aflibercept). The study, however, was not designed to determine the difference between aflibercept and ranibizumab. Only by performing a true as-needed (prn) study can a good comparison be made. VIEW was more of a pseudo-prn study in which all patients received injections at least once every 3 months, but more frequent injections were allowed if needed.

The mechanism of action for aflibercept is slightly different other anti-VEGF agents in that its soluble receptor binds to VEGF and also to platelet-derived growth factor. Aflibercept binds not only to a wider spectrum of molecules, but it binds with a higher affinity. How significant this difference is may be questionable, as the affinities of ranibizumab and bevacizumab (Avastin, Genentech) are already quite high.

Although I have begun using aflibercept in my practice since its approval, the issues of reimbursement and assignment of a J code must be addressed before I adopt this drug on a widespread basis. When ranibizumab was first approved, many clinicians experienced a large backlog of unpaid claims during the waiting period for that J code, and I do not want to have the same thing happen with aflibercept, particularly when we have a good anti-VEGF treatment at our disposal for which we can be reimbursed. Regeneron, however, has been proactive in providing information to help identify insurance companies that will cover the drug prior to the J code assignment.

Many of my patients have been receiving injections of ranibizumab or bevacizumab either monthly or every 6 weeks and still have had persistent fluid on optical coherence tomography (OCT). For these patients, aflibercept will offer an advantage with less frequent dosing.

The lower cost of aflibercept, particularly because its label calls for less frequent dosing, is quite remarkable. In my opinion, this strategy will prove to be a game-changer in terms of how new drugs are brought to market in the future. ■

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1. FDA approves Eylea for eye disorder in older people: Maintains clearness of vision in those with wet age-related macular degeneration. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm280601.htm. Accessed March 7, 2012.
2. Nguyen QD, Heier J, Brown D, et al. Randomized, double-masked, active-controlled phase 3 trial of the efficacy and safety of intravitreal VEGF trap-eye in wet AMD: one-year results of the View-1 study. *Invest Ophthalmol Vis Sci.* 2011;52:E-Abstract 3073.
3. Schmidt-Erfurth U, Chong V, Kirchof B, et al. Primary results of an international phase III study using intravitreal VEGF trap-eye compared to ranibizumab in patients with wet AMD (VIEW 2). *Invest Ophthalmol Vis Sci.* 2011;52:E-Abstract 1650.

the ranibizumab every 4 weeks group, in order to compare the recommended regimens for the 2 drugs.)

In year 2, the study design was a capped prn regimen across treatment and comparator arms.[9]

EFFICACY RESULTS

In VIEW 1, 1217 patients were randomized, and in VIEW 2, 1240 patients were randomized.[6,7] A total of 2412 patients in the 2 studies were treated and evaluated; 1817 were treated with aflibercept.[2] Mean patient age was 76 years.

The primary endpoint, maintenance of BCVA, was achieved at 1 year. As has been reported previously,[2] in the integrated analysis at 52 weeks, 94% and 95% of patients treated with 2 mg aflibercept every 8 weeks lost fewer than 3 lines of BCVA, as did 94% of patients treated