

FDA Approved Ranibizumab for Neovascular AMD

AMD is a major cause of blindness in individuals aged ≥ 55 years.

BY CONNI BERGMANN KOURY, EDITOR-IN-CHIEF

The US Food and Drug Administration (FDA) has approved ranibizumab injection (Lucentis; Genentech, San Francisco) for the treatment of neovascular or *wet* age-related macular degeneration (AMD). The approval comes on the heels of a 6-month priority review granted by the FDA. The company said the product has begun shipping to surgeons.

According to an FDA news release, ranibizumab is the first treatment, which, when dosed monthly, can maintain the vision of $>90\%$ of patients with this form of AMD. The agent is a new molecular entity, meaning it contains an active substance that has never before been approved for marketing in any form in the United States.

Ranibizumab binds to and inhibits the biologic activity of human VEGF-A.

BACKGROUND

Ranibizumab is a recombinant humanized IgG1 kappa isotype therapeutic antibody fragment developed for intraocular use. It binds to and inhibits the biologic activity of human vascular endothelial growth factor A (VEGF-A), a protein that is believed to play a critical role in angiogenesis. VEGF-A has been shown to lead to neovascular AMD disease progression and central vision loss.

"In my opinion, the Lucentis approval stands out as one of the most important medical developments in ophthalmology during my 25 years in the field because it has the potential to reverse vision loss associated with wet AMD," said Eugene de Juan, MD, president, American Society of Retina Specialists. "We are pleased that Lucentis has been approved by the FDA and look forward to working with Genentech to provide retina specialists in the United States with access to Lucentis for patients as quickly and smoothly as possible." Dr. de Juan is the Jean Kelly Stock Distinguished Professor in the University of California, San Francisco Department of Ophthalmology.

CLINICAL TRIALS

The FDA approved ranibizumab based on data from two large phase 3 clinical trials called MARINA (Minimally Classic/Occult Trial of the Anti-VEGF Antibody Ranibizumab in the Treatment of Neovascular AMD) and ANCHOR (Anti-VEGF Antibody for the Treatment of Predominantly Classic Choroidal Neovascularization in AMD). In these studies, approximately 95% of patients treated with ranibizumab 0.5 mg maintained visual acuity (defined as the loss of <15 letters) and $\leq 40\%$ improved vision (defined as the gain of ≥ 15 letters) at 1 year, as measured on the Early Treatment of Diabetic Retinopathy (ETDRS) eye chart.

On average, patients treated with ranibizumab in the MARINA study experienced an improvement from a baseline of 6.6 letters at 2 years compared with a loss of 14.9 letters in the sham-assigned group. In

the ANCHOR study, patients treated with ranibizumab, on average, experienced an 11.3-letter gain from baseline at 1 year compared with a loss of 9.5 letters in the verteporfin photodynamic therapy (Visudyne; Novartis, East Hanover, NJ) control group. Up to 40% of patients treated with ranibizumab achieved vision of 20/40 or better.

ELDERLY POPULATION INCREASING

“This approval is of great importance for the 155,000 Americans who are diagnosed each year with AMD, a common cause of severe and irreversible vision loss in older adults,” said Andrew von Eschenbach, MD, acting commissioner of Food and Drugs. “At a time when our elderly population is rapidly increasing, this product preserves quality of life for those affected by this disease, helping them regain the ability to participate in everyday activities such as reading and driving.”

Data from the FOCUS and PIER studies strengthened the approval process for ranibizumab.

In addition to data from the two pivotal studies, data from the phase 1/2 FOCUS (RhuFab V2 Ocular Treatment Combining the Use of Visudyne to Evaluate Safety) and phase 3b PIER studies (A Phase IIIb, Multicenter, Randomized, Double-Masked, Sham Injection-Controlled Study of the Efficacy and Safety of Ranibizumab in Subjects with Subfoveal Choroidal Neovascularization with or without Classic CNV Secondary to Age-Related Macular Degeneration) were included in the FDA review, according to Genentech.

INTRAVITREAL ADMINISTRATION

Ranibizumab 0.5 mg is recommended for intravitreal injection once a month. If monthly injections are not feasible, treatments can be reduced to one injection every 3 months after the first four monthly injections. Compared with continued monthly dosing, dosing every 3 months will lead to an approximate five-letter (one-line) loss of visual acuity benefit, on average, over the following 9 months. Patients should be evaluated regularly, according to the company.

“Now that Lucentis is approved, we will continue to work with the retina community to evaluate how

patients may be able to benefit from less frequent dosing, as emerging clinical data indicate that dosing may need to be tailored to individual patient needs,” said Arthur D. Levinson, PhD, Genentech’s chairman and CEO. “Lucentis provides new hope for patients with wet AMD because it is the first therapy to provide a benefit in vision for a significant number of patients. We are proud that the seminal work in angiogenesis conducted at Genentech, years of clinical study, and the dedication and commitment of thousands of patients and retina specialists have all contributed to this important approval.”

ADVERSE EVENTS

In clinical trials, the most common adverse reactions among patients treated with the agent (reported in $\geq 6\%$ more patients than in the control groups in at least one study) included conjunctival hemorrhage, eye pain, vitreous floaters, increased intraocular pressure (IOP) and intraocular inflammation. Although there was a low rate ($< 4\%$) of arterial thromboembolic events (ATEs) observed in the clinical trials that was not statistically different between the treatment and control groups, there is a theoretical risk of ATEs following intravitreal use of inhibitors of VEGF, according to the news release. Serious adverse events related to the injection procedure (ie, endophthalmitis, retinal detachments and traumatic cataracts) occurred in $< 0.1\%$ of intravitreal injections. Other serious ocular adverse events observed among some ranibizumab-treated patients ($< 2\%$) included intraocular inflammation and increased IOP.

Ranibizumab is contraindicated in patients with hypersensitivity and ocular or periocular infections.

“The impact of wet AMD goes beyond vision loss and can affect a person’s ability to interact with family and friends, conduct daily activities and, overall, maintain their independence,” said Stephen Rose, MD, chief research officer at the Foundation Fighting Blindness (Owings Mills, Md). “As an organization dedicated to research for preventions, treatments and cures for people affected by retinal degenerative diseases, we applaud the FDA’s approval of Lucentis as an important advancement in the treatment of wet AMD.” ■

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