

# Pegaptanib Safety Profile Maintained Through 2 Years

No increased risk of cardiovascular events was seen in patients with neovascular AMD; no additional safety concerns brought to light.

BY CONNI BERGMANN KOURY, EDITOR-IN-CHIEF

**T**he safety profile of pegaptanib (Macugen; OSI Eyetech, Melville, NY/Pfizer, New York, NY), established in data from the first year of the of the trials Vascular Endothelial Growth Factor (VEGF) Inhibition Study In Ocular Neovascularization (VISION), was maintained over 2 years of treatment. There was no evidence of an association with hypertension, serious hemorrhagic events or thromboembolic events as compared with the control group, according to a news release from the manufacturers.

Such events have been noted with the clinical use of other VEGF inhibitors. A preliminary analysis of a third year of data presented at the Macula Society meeting in Carlsbad, Calif, suggests that the safety of pegaptanib is maintained throughout 3 years of treatment.

## IMPORTANCE OF LONG-TERM DATA

"These long-term safety data are of utmost importance because wet [age-related macular degeneration] (AMD) afflicts people over the age of 65, an age group already at increased risk of cardiovascular disease, including heart attack and stroke," said Lawrence J. Singerman, MD, clinical professor of ophthalmology at Case University

School of Medicine and president of Retina Associates of Cleveland. "[Pegaptanib's] proven systemic safety profile over 2 years is encouraging because many of our patients require long-term treatment since AMD is a chronic, progressive disease."

Pegaptanib is the only VEGF inhibitor with long-term safety data in neovascular AMD, and the only



Photo courtesy of the National Eye Institute, National Institutes of Health

Figure 1. This fundus photo shows a normal retina.

## PEGAPTANIB: PAVING THE WAY FOR FUTURE APTAMER APPLICATIONS?

*Pegaptanib represents the first available aptamer approved for human use. It is also the first ophthalmic drug that has been approved for all types of neovascular AMD.*

As an aptamer, pegaptanib specifically targets VEGF<sub>165</sub>. Aptamers are single-stranded nucleic acids that form well-defined 3-D shapes, binding target molecules in a manner conceptually similar to antibodies, according to the manufacturers. These aptamers have desirable characteristics for use in therapeutics, such as biological efficacy, high specificity and affinity and flexible pharmacokinetic properties.

Aptamers are different from antibodies. They are reasonably simple and inexpensive to synthesize commercially as opposed to antibodies, which are more complex to manufacture. They are also relatively small chemically synthesized molecules, free from cell-cultured contaminants. They rarely elicit an immune response, even if administered in excess of therapeutic doses. This is not true of monoclonal antibodies.

There are many potential applications of aptamers as therapeutic agents in the pipeline, including cancer and anticoagulation. The combined administration of aptamers may be something that yields a more potent effect than a single aptamer, and it is also being investigated.

Ng EW, Shima ST, Calias P, et al. Pegaptanib, a targeted anti-VEGF aptamer for ocular vascular disease. *Nat Rev Drug Discov.* 2006;2:123-132.

VEGF inhibitor that specifically targets VEGF<sub>165</sub>, the isoform primarily responsible for promoting the blood vessel growth and leakage associated with neovascular AMD, according to a news release.

Pegaptanib specifically targets VEGF<sub>165</sub>, the isoform responsible for promoting blood vessel growth and leakage in AMD.

Dr. Singerman presented data from two pegaptanib trials, jointly named VISION, that were concurrent multicenter, double-masked, randomized, controlled studies, which enrolled 1,190 patients. At the beginning of the second year, patients receiving pegaptanib 0.3 mg, 1 mg or 3 mg were rerandomized in a 1:1 ratio to either continue treatment for an additional 48 weeks or to discontinue treatment. Sham-assigned patients were also rerandomized to either receive one of the three pegaptanib doses, continue in the sham group or discontinue treatment.

#### NO INCREASE IN ADVERSE EVENTS

The 2-year systemic safety data examined the 425 patients (0.3 mg, n=128; 1 mg, n=126; 3 mg, n=120; sham, n=51) who continued the same treatment in the

second year as in the first.

These patients received a total of 2,663 intravitreal injections of pegaptanib and 388 sham injections. The systemic safety profile established in year 1 was sustained in year 2. There was no evidence that pegaptanib was associated with an increased incidence of adverse events, such as systemic hypertension, serious hemorrhagic events or thromboembolic events compared with the control group.

After 2 years, patients receiving pegaptanib 0.3 mg or 1 mg continued on the same dose for a third year; all remaining subjects were rerandomized either to 0.3 or to 1 mg for a third year. A total of 422 patients entered into the third year of the VISION trials. Of these, 161 patients received pegaptanib for 3 years. Dr. Singerman reported that the safety profile was maintained.

Pegaptanib has been approved by regulatory authorities in the United States, European Union, Canada, Brazil, Argentina, Peru, Pakistan, the Philippines and Switzerland, with filings submitted in 14 other countries. ■

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Singerman LJ. Safety data and preliminary 3-year results from VISION. Presented at the annual Macula Society meeting, Feb. 22 to 25, 2006, Carlsbad, California.