The ability of vascular endothelial growth factor (VEGF) inhibitors to improve visual acuity in most patients with neovascular age-related macular degeneration (AMD) has been well established in clinical trials and clinical practice. In most of these patients, however, choroidal neovascularization (CNV) is stabilized but does not regress. Anti-VEGF drugs control angiogenesis and leakage, but they do not effect vascular remodeling.

Platelet-derived growth factor (PDGF) is a protein that regulates cell growth and is involved in angiogenesis. An anti-PDGF pegylated aptamer (E10030, Ophthotech) has been shown in experimental models of neovascularization to “strip away” pericytes from neovascular tissue.1,2

A phase 1 clinical trial was conducted to evaluate intravitreal combination therapy of the PDGF inhibitor E10030 plus the VEGF inhibitor ranibizumab (Lucentis, Genentech).3 This dose-escalation study included 22 patients at multiple sites, with 0.03-, 0.3-, 1.5-, and 3.0-mg doses of E10030 given in combination with ranibizumab once monthly for 3 months. All eyes in the study had subfoveal CNV with some classic component and a total lesion size of five disc areas or less. Pre- and post-treatment fluorescein angiography were analyzed for CNV vascular area and qualitative patterns.

Results of this phase 1 study were compared with a retrospective group of 24 patients treated with ranibizumab or bevacizumab (Avastin, Genentech) induction therapy, once a month for 3 to 5 months, from 2007 to 2009.3 These patients had mostly predominantly classic CNV lesions secondary to AMD with total lesion size of five disc areas or less.

With anti-PDGF/anti-VEGF combination therapy, partial regression of CNV lesions occurred in 91% of patients. Vascular regression of CNV was observed to leave a hypo-fluorescent plaque. No patients receiving combination therapy experienced progression of CNV in the trial. In contrast, in patients treated with anti-VEGF monotherapy, CNV regressed in 16% of patients, but most remained stable and some progressed. Stable inactivity was observed in 9% of eyes treated with combination therapy, compared with 68% of eyes treated with anti-VEGF monotherapy.

These preliminary data suggest that combination therapy with an anti-PDGF aptamer plus a VEGF inhibitor produces regression of CNV lesions. Fluorescein and indocyanine green angiography is useful in evaluating the regression of CNV lesions in response to treatment.

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3. Cousins SW, Csaky KG, Ophthotech Study Group. Patterns of CNV fluorescein and indocyanine green angiographic regression responses after anti-VEGF monotherapy or anti-VEGF plus anti-PDGF combination therapy. Paper presented at: Association for Research in Vision and Ophthalmology annual meeting; May 4, 2009; Fort Lauderdale, FL.