

Expanding Ophthalmologic Indications for the use of Bevacizumab

Bevacizumab (trade name Avastin) is a humanized recombinant monoclonal IGG antibody developed by Genentech that binds to all known forms of human vascular endothelial growth factor (VEGF). Once bound by the Avastin molecule, the biologic activity of VEGF has been proven to be markedly inhibited in both in vitro and in vivo assays. Avastin was initially studied as an angiogenic inhibitor of tumor vascularization and was found to be effective in decreasing the vascular supply to a variety of metastatic lesions. For this reason, it has been given formal FDA approval for treatment of patients with carcinoma of the colon and rectum in addition to patients with metastatic unresectable lung cancer and those with HER2-negative metastatic breast cancer.

Because of its well-documented anti-angiogenic effectiveness and its similar mechanism of action to ranibizumab (trade name Lucentis), a smaller humanized monoclonal antibody specifically developed by Genentech to treat neovascular macular degeneration, Avastin was also contemplated as a treatment for choroidal neovascular activity. In 2005, intravitreal injections of Avastin were performed on patients with subfoveal choroidal neovascular membranes by Philip Rosenfeld, MD at the University of Miami as an off-label salvage indication since Lucentis had not yet been FDA-approved for use. These initial 40 patients demonstrated an encouraging response to the Avastin injections which appeared to be essentially similar to that described for Lucentis. For this reason, and since at that time Lucentis was not expected to be approved for several more months, the use of intravitreal Avastin treatment of neovascular macular degeneration spread rapidly throughout the world. Since then, Avastin has become a mainstay of therapy for neovascular macular degeneration accounting for up to 50% of treatments for subfoveal membranes (Lucentis accounts for most of the remainder). Both Avastin and Lucentis appear to have a 90-95% rate of vision stability with ongoing treatment as well as a 40% rate of visual improvement in less extensive lesions.

Buoyed by the successful use of Avastin in macular degeneration and based on its ability to significantly reduce fluid leakage in choroidal neovascular activity, a number of small clinical trials were completed in which Avastin was used to treat a variety of vascular processes associated with the production of macular edema. The first entity treated was central retinal vein occlusion (CRVO) which typically has a poor visual prognosis in those patients where significant edema develops over time especially in the presence of ischemia. The initial results were quite encouraging with many patients demonstrating a reduction in macular edema as well as visual improvement.

As a result of these promising findings in CRVO, patients with branch retinal vein occlusion were treated with similar impressive results. Avastin use in diabetic macular edema and proliferative retinopathy has also recently been demonstrated to be effective in certain cases and it may be that most retinal vascular processes resulting in either neovascular activity or macular edema will eventually be found to respond to anti-VEGF treatment.

Medicare and most insurance companies now cover the use of Avastin in wet macular degeneration, diabetic retinopathy and retinal venous occlusions and have more recently expanded the list of disorders allowed for reimbursement to include neovascular glaucoma, choroidal neovascularization not associated with macular degeneration and other forms of non-diabetic proliferative retinopathy.

At North Bay Vitreoretinal Consultants, we are currently using Avastin in retinal vascular occlusive disease as well as in diabetic retinopathy as an adjunct to laser in the treatment of diabetic macular edema and neovascularization. We have had success using Avastin for treatment of choroidal neovascular activity associated with angioid streaks and degenerative myopia. The macular edema and exudate caused by Coat's Disease and Idiopathic Juxtafoveal Telangiectasia have also been found to be responsive to Avastin in our practice.

Considering that just five years ago the most effective treatment we could offer patients with subfoveal choroidal neovascular membranes was treatment with thermal laser (which inevitably left patients with significant central scotomata) or photodynamic therapy (better than thermal laser but with limited success at best), the advent of anti-VEGF agents has been remarkable in its efficacy and the rapidity in which our paradigm for treatment of macular degeneration has been altered. We're now seeing a similar global process evolving in our treatment of other retinal vascular disorders. It is exciting and gratifying that we can finally offer hope to patients with these otherwise blinding conditions.