



#### Young EVRS Column

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### **Intravitreal Bevacizumab (Avastin) For The Treatment Of Retinovascular Diseases**

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Ocular neovascularization and increased vascular permeability have been associated with Vascular Endothelial Growth Factor (VEGF), a diffusible cytokine that plays a key role in the process of normal and pathologic angiogenesis. Animal studies have demonstrated that VEGF expression is able to promote neovascularization in the eye, whereas its inhibition reduces its effect. In addition, the presence of VEGF is temporally and spatially correlated with ocular angiogenesis in the primate model. Increased intravitreal levels of VEGF have been observed in many retinovascular diseases such as proliferative diabetic retinopathy, age-related macular degeneration, retinopathy of prematurity and retinal vein occlusion.

One possible therapeutic approach to the development of abnormal blood vessels in proliferative diabetic retinopathy and central retinal vein occlusion, choroidal neovascularization secondary to age related macular degeneration, and macular edema associated to various retinovascular diseases is to inhibit VEGF activity with a VEGF-blocking drug.

Bevacizumab (Avastin; Genentech) is a full-length humanized murine monoclonal antibody against VEGF approved by the Food and Drug Administration for treating metastatic colorectal cancer. Ranibizumab (Lucentis, Genentech) is an antibody fragment of Bevacizumab whose potential advantage over the whole antibody is the smaller molecule size that should allow a better penetration of the drug through all the retinal layers.

Systemic administration of Bevacizumab has been used for the treatment of eyes affected by neovascular age-related macular degeneration: visual acuity improvement and remarkable regression of macular changes on optical coherence tomography and fluorescein angiography were demonstrated.<sup>1</sup> However, the intravenous use of Bevacizumab can have serious systemic side effects such as thromboembolia, systemic hypertension, epistaxis, hemoptysis, proteinuria, wound healing complication, gastrointestinal hemorrhage and others.

In order to decrease these adverse events the intravitreal injections of Bevacizumab has been proposed. The intravitreal dosage of Bevacizumab is 1.25 mcg/0.05 cc., 400 fold less than the systemic dose. The cost of the injection is only about €6.00.

Intravitreal Bevacizumab has been described in some recent articles for the treatment of proliferative diabetic retinopathy complicated by vitreous hemorrhage,<sup>2</sup> macular edema in central retinal vein occlusion,<sup>3</sup> and neovascular age-related macular degeneration.<sup>4</sup> Initial treatment results showed a significant regression of neovascularization, decrease in macular edema, and improvement in visual acuity. Published data on retinal toxicity suggests that there is no significant measurable photoreceptor toxicity with the use of intravitreal Bevacizumab over the short term.<sup>5</sup>

Bevacizumab was not created to be administered intravitreally, intraocular injection of the drug is an off-label procedure. As a consequence some retinal specialists are taking a wait-and-see approach waiting for more literature data on safety, efficacy and toxicity, while others are using Bevacizumab as a salvage therapy in patients who continue to lose vision despite treatment with approved therapies.

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In spite of the promising results of intravitreal Bevacizumab for the treatment of various retinovascular diseases, further studies are required to evaluate the long-term efficacy and safety of this drug.

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