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Pegaptanib in Exudative Age-Related Macular Degeneration

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Neovascular or wet age-related macular degeneration (AMD) is responsible for severe irreversible visual loss within a short time, if untreated. Until recently, the only proven treatment for this condition (and other types of choroidal neovascularisation [CNV]) was laser photocoagulation. However, laser photocoagulation was useful only in extrafoveal lesions and there was a 50% recurrence in 2 years. Fortunately, we can now treat some types (predominantly classic and occult) of subfoveal CNV with photodynamic therapy (PDT). PDT has to be repeated 3 monthly for about 2 years. There also remains a significant number of CNVs (minimally classic) for which PDT is less efficacious. The search for the 'optimum treatment' for CNVs, therefore, continues.

It is now accepted that growth factors, principally vascular endothelial growth factor (VEGF), play a significant role in the development and growth of CNV and other intraocular vasoproliferation, and vascular leakage (e.g. diabetic retinopathy and vein occlusions). Therefore, it is logical that one of the treatment modalities currently under investigation for treatment of wet AMD is blockage of VEGF in the eye. Of course, this does not treat the underlying pathology.

Randomised clinical trials have shown that repeated 6 weekly intravitreal injections of pegaptanib (Macugen®)[1] in eyes with CNV preserves vision over 2 years. Direct delivery of the drug to the diseased organ has significant appeal since maximal concentrations are achieved with minimal systemic toxicity. So far, the injections seem well tolerated in human eyes, with minimal toxic potential in the eye or systemically. The most significant ocular adverse effect was endophthalmitis. However, its incidence was reduced considerably when the injection protocol was modified with adequate attention to asepsis. Thus, with strict adherence to aseptic delivery, endophthalmitis should not be a problem.

The main disadvantage of pegaptanib is the repeated delivery every 6 weeks for an indefinite period. Protocols that require less frequent delivery need evaluation. However, the most significant advantages will be achieved if a slow-release delivery by an intravitreal implant similar to gancyclovir or fluocinolone is developed. Alternatively, subtenon's delivery may need exploration since this route will be more appealing to some clinicians. Combination therapy with other treatment modalities, e.g. pegaptanib and PDT, as practiced in cancer care, may increase efficacy, reduce frequency of administration and toxicity as well as the need for prolonged treatment periods. This hypothesis, of course, needs to be tested.

Pegaptanib may also have a role, albeit in the short-term, in the management of diabetic maculopathy or macular oedema in retinal vein occlusions where reduction of vascular leakage is required as a supplement to other treatments including laser photocoagulation. Pegaptanib and other anti-VEGF agents are welcome additions to the ophthalmologist's arsenal and, in combination with other agents, will play a major role in the management of CNV and retinal vascular diseases in the future. ▲

1 The use of trade names is for product identification purposes only and does not imply endorsement.