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Ranibizumab

A Viewpoint by Winfried Amoaku

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Neovascular age-related macular degeneration (AMD) is responsible for severe irreversible visual loss within a short time if untreated. We can treat some types (predominantly classic and occult) of subfoveal choroidal neovascularisation (CNV) with photodynamic therapy (PDT). However, PDT has to be repeated 3 monthly for about 2 years; it is palliative, and visual loss still occurs, albeit at a slower rate compared with no treatment. There also remains a significant number of CNVs (minimally classic and large occult) for which PDT is less efficacious or even detrimental.

As vascular endothelial growth factor (VEGF), principally, and other growth factors play a significant role in the development and growth of CNV and vascular leakage, it is logical that selective inhibition of VEGF in the eye is a therapeutic target. Pegaptanib, the first anti-VEGF treatment for CNV,[1] has similar efficacy to that of PDT. The more recent introduction of ranibizumab represents a further advance in anti-VEGF therapy for CNV. Unlike pegaptanib, which only inhibits $VEGF_{165}$, ranibizumab inhibits all active isoforms of VEGF-A.

Randomised, controlled trials have shown that repeated intravitreal injections of ranibizumab 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. The injections seem well tolerated in human eyes. Visual acuity improved in 25–40% of patients receiving ranibizumab and was maintained in 94–96%, compared with 5% and 65%, respectively, with PDT. The 0.5mg dose is more effective than the 0.3mg dose. There have been no direct comparisons between ranibizumab and pagaptanib. However, ranibizumab seems to be the more effective. As such, ranibizumab represents the first treatment that has consistently preserved and improved vision in eyes with CNV over a 2-year period. Serious ocular adverse effects of endophthalmitis, retinal detachment and lens damage were rare in all the trials. Thus, with strict adherence to asepsis, and delivery by trained ophthalmologists, serious adverse events should not be a problem. Systemic adverse effects occurred no more frequently with ranibizumab than with placebo.

The main disadvantage of ranibizumab is the repeated delivery every 4 weeks for an indefinite period, as there seems to be a slight risk of recurrence of the CNV after 2 years. Protocols that require less frequent delivery, without loss of efficacy, need evaluation. Combination therapy with other treatment modalities, e.g. ranibizumab and PDT, may increase efficacy, and reduce frequency of administration and toxicity, as well as the need for prolonged treatment periods. This hypothesis is supported by preliminary investigations.[2,3]

Ranibizumab and other anti-VEGFs 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. ▲

References

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