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Ranibizumab

A Viewpoint by Thomas A. Ciulla

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Age-related macular degeneration (AMD) is the leading cause of irreversible visual loss in the industrialised world. Most of the cases of legal blindness result from the exudative form, in which vascular endothelial growth factor (VEGF) is secreted in the choroid leading to choroidal neovascular (CNV) membranes, central macular scarring and legal blindness. In an aging society, this disorder has enormous public health implications. There was no visual restorative treatment available until intravitreal ranibizumab, a monoclonal antibody antigen-binding fragment that targets all isoforms of VEGF and their smaller bioactive cleavage products, received US FDA approval for the treatment of neovascular AMD in 2006.

The two pivotal phase III trials that led to FDA approval of ranibizumab, MARINA and ANCHOR, showed that monthly intravitreal ranibizumab for 2 years was associated with significant improvements in visual acuity, compared with either sham treatment or verteporfin photodynamic therapy. The MARINA trial design investigated monthly intravitreal ranibizumab (0.3 or 0.5mg) in minimally classic or occult with no classic CNV secondary to AMD. The ANCHOR study compared monthly intravitreal ranibizumab (0.3 or 0.5mg) with sham verteporfin photodynamic therapy versus verteporfin therapy with sham ranibizumab injection in patients with predominantly classic CNV secondary to AMD. Twelve-month results for both MARINA and ANCHOR showed that significantly greater proportions of ranibizumab-treated patients (94–96%) had lost <15 letters of visual acuity, compared with 62–64% of control patients ($p < 0.001$). Also at 12 months, 25–40% of ranibizumab recipients had gained ≥15 letters of visual acuity, compared with 5–6% of control patients ($p < 0.001$). Two-year results from MARINA were similar, with ranibizumab-treated patients achieving significantly greater improvements in visual acuity than patients in the control group. Together, the MARINA and ANCHOR trials established ranibizumab as the first therapeutic agent to not only prevent vision loss, but also to improve vision in a substantial proportion of patients with all subtypes of CNV secondary to AMD.

Additional clinical studies of alternative dosing strategies of ranibizumab, such as the PIER (monthly ranibizumab injections for 3 months then quarterly) and the PrONTO (optical coherence tomography-guided, variable dosing regimen) studies, have also provided data supporting the benefits of ranibizumab in patients with neovascular AMD. These alternative dosing studies demonstrate that ranibizumab can be utilised effectively to halt visual loss, and in some cases improve visual acuity, without monthly injections. Further studies are being conducted to assess various combinations of therapies with ranibizumab and other anti-VEGF agents in order to address the enormous public health implication of exudative AMD, a disorder that will become increasingly prevalent as our society ages. ▲