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Comments on Standardized visual acuity results associated with primary versus secondary bevacizumab (avastin) treatment for choroidal neovascularization in age-related macular degeneration

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Dear Editor

We appreciate the interest of Uparkar et al in our recent study.[1] We agree with them that standardized visual acuity measurements with Early Treatment Diabetic Retinopathy Study charts are important in evaluating any vision changes after treatment. This is particularly true in the low-vision range of patients with age-related macular degeneration, for whom Snellen charts are inaccurate.

We are asked to provide additional information on our patients and to explain why the secondary bevacizumab (Avastin; Genentech, Inc., South San Francisco, CA) group had a mean number of injections of 4.2 (range, 2–7). Uparkar et al have misread our report. The group with the mean number of injections of 4.2 (range, 2–7) was the eyes initially treated with pegaptanib (Macugen; Eyetech Pharmaceuticals, New York, NY). These data relate to the number of pegaptanib injections, not the number of bevacizumab injections. This appears to be clearly stated in paragraph 4 under Methods and Participants. We wish to point out that both the eyes in the primary bevacizumab group and the eyes treated with bevacizumab after failing to respond to pegaptanib had similar bevacizumab treatment courses (mean number of injections: secondary bevacizumab [salvage therapy] group, 3.8; primary bevacizumab group, 3.6). Despite the similar regimen, only the eyes in the primary bevacizumab group improved. This suggests that salvage therapy with bevacizumab for eyes failing to improve after pegaptanib injections may not be possible.

The questions of Uparkar et al also seem to imply that this was a controlled study of two similar groups. This was not the case. Obviously, eyes that did not respond to pegaptanib treatment are not the same as treatment-naive eyes. The question, however, as to whether eyes that fail to respond to pegaptanib will respond to bevacizumab (or Lucentis [ranibizumab]; Genentech, Inc.) is highly relevant because there are many patients who did not have improved vision after pegaptanib therapy. Indeed, such patients are the rule rather than the exception. We attempted to answer the question as to whether such eyes might have visual improvement after bevacizumab treatment. Unfortunately, it appears that attempts at salvage therapy with bevacizumab are not successful in improving vision despite the fact that there is a reduction in retinal thickness after changing treatment from pegaptanib to bevacizumab.

Clinical trials have already demonstrated that vision improvement after pan–vascular endothelial growth factor blockade such as is seen with bevacizumab or ranibizumab is superior to that after partial vascular endothelial growth factor blockade that is seen with pegaptanib. Indeed, vision improvement is not usually seen with pegaptanib treatment, although it is the rule after either bevacizumab or ranibizumab injection. The only purpose of our study was to determine whether the more superior drugs, which block all isoforms of vascular endothelial

growth factor, could improve vision after failure to do so with pegaptanib. It appears that they cannot.

The reason why the bevacizumab-associated reduction in retinal thickness in cases of failure of pegaptanib treatment is not associated with vision improvement is unclear. One may speculate that during pegaptanib therapy there is ongoing damage to the neurosensory retina, which cannot be overcome by delayed treatment with the more effective drug. It is for these reasons that we no longer use pegaptanib in our clinical practice.

References

1. Falkenstein IA, Cheng L, Morrison VL, et al. Standardized visual acuity results associated with primary versus secondary bevacizumab (Avastin) treatment for choroidal neovascularization in age-related macular degeneration. Retina 2007;27:701–706. [PubMed: 17621178]