



Published in final edited form as:

*JAMA Ophthalmol.* 2015 June ; 133(6): 726. doi:10.1001/jamaophthalmol.2015.0502.

## Analyses Comparing Visual Acuity Between Ranibizumab and Bevacizumab in the Comparison of Age-Related Macular Degeneration Treatments Trials

Gui-shuang Ying, PhD and Maureen G. Maguire, PhD

Department of Ophthalmology, Scheie Eye Institute, Perelman School of Medicine, University of Pennsylvania, Philadelphia

### To the Editor

We thank Dr Messori<sup>1</sup> for the interest in our 2 articles from the Comparison of Age-Related Macular Degeneration Treatments Trials.<sup>2,3</sup> Dr Messori believes that results in the 2 articles for comparison of visual acuity between eyes treated with bevacizumab and eyes treated with ranibizumab are contradictory.<sup>1</sup> Dr Messori speculates that analyzing visual acuity change from baseline as a dichotomous variable (sustained loss of 15 letters) in the article on sustained visual acuity loss<sup>3</sup> but as a continuous variable (mean change in visual acuity from baseline) in the article on the 2-year main results<sup>2</sup> may be responsible for the apparent contradiction. We believe there is no contradiction because the objectives of the 2 articles were different and because different approaches to data analysis were warranted.

For the article on the 2-year main results, the relevant objective was to compare “ranibizumab and bevacizumab when administered monthly or as needed for 2 years.”<sup>2</sup> The primary outcome measure for the clinical trial was mean change in visual acuity at 2 years. The magnitude of change, both positive and negative, for each eye contributed to the mean and we believe, as does Dr Messori, that the mean is the best summary measure for comparison to determine overall treatment effect. Only the 778 patients following the same dosing regimen (injections either monthly or as needed) for 2 years were included for this analysis; 252 patients who switched the dosing regimen from monthly to as needed (by study design) at the end of year 1 were not included. The mean change in visual acuity for eyes treated with bevacizumab was not different from eyes treated with ranibizumab (1.4 letters less for bevacizumab; 95% CI, 3.7 letters less to 0.8 letters more;  $P = .21$ ).

For the article on sustained visual acuity loss, the objective was “to determine the incidence, characteristics, causes, and baseline predictors of sustained visual acuity loss after 2 years of treatment.”<sup>3</sup> The definition of sustained visual acuity loss required at least a 15-letter loss

---

**Corresponding Author:** Gui-shuang Ying, PhD, Department of Ophthalmology, Scheie Eye Institute, Perelman School of Medicine, University of Pennsylvania, 3535 Market St, Ste 700, Philadelphia, PA 19104 (gsying@mail.med.upenn.edu).

**Conflict of Interest Disclosures:** All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr Ying reported having received a consulting fee from Janssen Research and Development LLC outside this work. No other disclosures were reported.

**Role of the Funder/Sponsor:** The funder had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

from baseline not only at 2 years but also at the preceding visit with a protocol visual acuity measurement. All 1030 patients treated under any of the dosing regimens (monthly for 2 years, as needed for 2 years, or switched from monthly to as needed at the end of year 1) were included. Patients treated with bevacizumab were more likely to have a sustained loss in visual acuity than those treated with ranibizumab (approximately 7.4% vs 4.6%, respectively; adjusted odds ratio = 1.83; 95% CI, 1.07–3.14;  $P = .03$ ). We agree with Dr Messori that dichotomizing the visual acuity change leads to loss of information on the overall effects of the drugs on visual acuity because the exact size of the change in visual acuity for each eye is not considered in this comparison.

## Acknowledgments

**Funding/Support:** This study was supported by cooperative agreements U10 EY017823, U10EY017825, U10 EY017826, U10 EY017828, and R21EY023689 from the National Eye Institute.

## References

1. Messori A. Comparative effectiveness of bevacizumab and ranibizumab in the Comparison of Age-Related Macular Degeneration Treatments Trials. *JAMA Ophthalmol.* [published online November 27, 2014]. 10.1001/jamaophthalmol.2014.4642
2. Martin DF, Maguire MG, Fine SL, et al. Comparison of Age-Related Macular Degeneration Treatments Trials (CATT) Research Group. Ranibizumab and bevacizumab for treatment of neovascular age-related macular degeneration: two-year results. *Ophthalmology.* 2012; 119(7): 1388–1398. [PubMed: 22555112]
3. Ying GS, Kim BJ, Maguire MG, et al. CATT Research Group. Sustained visual acuity loss in the comparison of age-related macular degeneration treatments trials. *JAMA Ophthalmol.* 2014; 132(8): 915–921. [PubMed: 24875610]