Dear Editor,

We read with great interest the article by Rush et al.1 The authors assessed, for the first time, the effectiveness and direct cost of intravitreal bevacizumab (IVB) (Avastin; Genentech, South San Francisco, CA) delivered in a treat-and-extend (TAE) regimen for patients with macular edema (ME) secondary to branch retinal vein occlusion (BRVO) during the course of 12 months. They concluded that IVB employed in a TAE algorithm resulted in similar visual outcomes and a similar number of intravitreal injections compared with the pro re nata (PRN) approach with 0.5 mg ranibizumab (Lucentis; Genentech, South San Francisco, CA) during the phase 3 BRAVO trial,2 but with fewer visits and lower annual medical costs.

However, there are some issues we would like to address. Firstly, the comparison between the current study results1 and those of the BRAVO trial2 was totally inappropriate because there was a definite difference in the evolution stages of the disease between the two studies. Thus, patients in the current study had a significantly less-progressed disease (ie, thinner macula, better visual acuity, and earlier diagnosed disease).

Secondly, there was a discrepancy between visual and structural outcomes in the current study. Despite remarkable visual improvements in the best-corrected visual acuity after treatment, the structural outcomes were poor. Unresolved ME was observed in 33 out of the 52 patients, which indicated that the disease process was still active and progressive. Edematous macular changes are manifestations of a permanent retinal capillaropathy,3 a condition caused by ischemic lesions of the macular retinal ganglion cells close to the foveola. Presumably, these damages appeared during the period of time when the patients went without treatment (ie, before beginning the treatment), because therapy was initiated within 6 months (mean: 1.6) of BRVO onset when the amount of vascular endothelial growth factor (VEGF) was maximally expressed.

Additionally, reverting to more intensive treatment is mandatory for all patients with unresolved ME after careful review of the optical coherence tomography (OCT) and/or angiography data. If disease activity increases (eg, fluid recurs on OCT/leakage on angiography), the injection interval should be shortened by 1 to 2 weeks. In the case of recurrent and persistent fluid, reinduction with monthly injection may be considered.4 Alternative strategies for severe deterioration include laser photoagulation and/or switching to the PRN treatment algorithm.

In conclusion, regardless of the anti-VEGF agents used (ranibizumab/bevacizumab), and regardless of the treatment approaches chosen (TAE/PRN algorithm), the efficacy of therapy depends primarily on the precociousness of the therapy after BRVO diagnosis.5

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REFERENCES

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Reply to Letter to the Editor: Treat-and-Extend Intravitreal Bevacizumab for Branch Retinal Vein Occlusion

Dear Editor,

The comparison of our current study results to those of the BRAVO trial was not totally inappropriate, as Drs. Dan and Mihai Călugăru alleged, because the BRAVO trial is the standard to which all treatment algorithms for branch retinal vein occlusion (BRVO) must be compared in order to deem their relative effectiveness. The differences in baseline characteristics between our study population and the BRAVO study population were explicitly pointed out in the first paragraph of our “Discussion” section, and this provides the reader with the necessary framework and perspective to interpret the merits of our treat-and-extend (TAE) protocol.

We are in strong disagreement with Drs. Dan and Mihai Călugăru that our structural outcomes were poor. Our study subjects experienced a mean final central macular thickness of just 246 µm (far below the 300 µm threshold considered by virtually all other studies as the cut-off for the presence of significant macular edema), with a mean change in central macular thickness of −244 µm by the study’s end. We consider these values to be indicative of excellent structural outcomes.

There was not unresolved macular edema in 33 out of the 52 patients at the end of our study, as Drs. Dan and Mihai Călugăru have stated. In fact, we explicitly stated in the first paragraph of the “Results” section that 33 out of the 52 patients required injections less frequently than 12 weeks by the study’s end, and that only nine of the 52 patients had recurrent or persistent macular edema evident on optical coherence tomography by the study’s end.

We agree with Drs. Dan and Mihai Călugăru that reverting to more intensive treatment is required for unresolved macular edema, and this is exactly what our TAE protocol dictated for persistent or recurrent macular edema; when persistent or recurrent macular edema was evident, our TAE protocol always required a shortening of the treatment interval (unless the subject was already at the 4-week treatment interval, in which case, the subject was maintained at monthly treatments until the macular edema resolved).

We also agree with the conclusion statement made by Drs. Dan and Mihai Călugăru.

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