Sir,
Comment on: 'Intravitreal aflibercept for macular oedema secondary to central retinal vein occlusion in patients with prior treatment with bevacizumab or ranibizumab'

In their article, Papakostas *et al*[1] assessed the efficacy of aflibercept (Eylea, Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA) in patients with macular edema (MO) secondary to central retinal vein occlusion (CRVO) resistant to bevacizumab (Avastin, Genentech, Inc., San Francisco, CA, USA) or ranibizumab (Lucentis, Genentech, Inc., South San Francisco, CA, USA). The authors concluded that converting eyes to aflibercept can result in stabilization of the vision, improved macular anatomy, and extension of the injection interval.

However, the study has several shortcomings, which prevent the validation of their results:

1. The study was retrospectively conducted with the possible existence of a bias. Thus, 24% of the cases had prior panretinal photocoagulation and 7% had previous steroids injections. In addition, treatment schemes, injection intervals, and injection techniques were at the discretion of each retina specialist.
2. The median central retinal thickness (CRT) at the end of the follow-up was 279 μm, a value proving persistent MO (defined as CRT greater than 250 μm[1]) requiring further treatment with anti-angiogenic agents.
3. The number of on average six injections of either bevacizumab or ranibizumab before the switch to aflibercept in 12 months is insufficient to label a patient as non-responder. The standard injection schemes during the first year of treatment were clearly set by the clinical trials, that is, injections given every 6 weeks for 48 weeks for bevacizumab[2] and six monthly injections followed by as needed administration for ranibizumab.[3]
4. The poor visual and anatomic outcomes of this series[1] (a gain of approximately five Early Treatment Diabetic Retinopathy Study letters in visual acuity; persistent macular edema in 45% of cases, and significant thinning of the retina (macular fibrosis? epiretinal membrane formation?) in 16.6% of cases) could be explained by the low frequency of injections, the period of time without therapy (a median of 1.25 months) before the start of any kind of treatment, and the period of time (12 months) when the patients were insufficiently treated with bevacizumab/ranibizumab. These findings favored the delayed occurrence of ischemic and irreversible damages of the macular ganglion cell complex, close to the foveola, because the vascular endothelial growth factor (VEGF) was maximally expressed during the first year of CRVO onset.

Our prospective clinical study[4,5] showed that regardless of the anti-VEGF agents used, the response to therapy depends primarily on the precociousness of the treatment after CRVO occurrence.

Conflict of interest

The authors declare no conflict of interest.

Authors contribution

DC and MC were involved in design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript.

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We would like to thank Călugăru and Călugăru[1] for their comments on our article.[2] We agree with them regarding the limitations of the study (retrospective nature, prior laser photocoagulation and/or steroid injections, different injection schemes), which were noted in our discussion.

They mention that a thickness of 279 μm signifies macular oedema requiring further treatment. We agree