**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 $\mu$m, a value proving persistent MO (defined as CRT greater than 250 $\mu$m[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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**Sir,**
**Reply to 'Comment on: Intravitreal aflibercept for macular oedema secondary to central retinal vein occlusion in patients with prior treatment with bevacizumab or ranibizmab'**

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 $\mu$m signifies macular oedema requiring further treatment. We agree

and for this reason the patients are continuing to receive treatment with intravitreal aflibercept injections. This study provides a real-life clinical experience with a switch to aflibercept in eyes with resistant or recalcitrant macular oedema secondary to central retinal vein occlusion.

In addition, they mention that an average of six injections (actually our study cohort had a median of seven) of bevacizumab or ranibizumab is insufficient to label a patient as a non-responder, claiming standard protocol used in studies. However, there is no consensus on the number of injections that designate a patient as a non-responder. Bhisitkul *et al*,[3] using data from the CRUISE study, classified patients as early responders (*vs* late or non-responders) based on OCT thickness $<250\,\mu$m 3 months after initiation of treatment. As our study reflects real-life practices, physicians used their own discretion to designate a patient as a poor on non-responder after no less than three injections as stated in the paper and in the example in Figure 4.

They also believe that the poor anatomic and visual benefits presented in our patients can be attributed to the low frequency of injections, the period of time without therapy (a median of 1.25 months before the initiation of treatment), and the period of time when the patients were insufficiently treated with bevacizumab/ranibizumab (12 months). We do not think that the delay in treatment by a median of 1.25 months adversely affected the outcome, as patients who were enroled in the CRUISE study[4] had also a median of 2 months from diagnosis to screening. In our study, the mean interval of injections before the switch was 5.6 weeks and after the switch was 7.6 weeks, as the majority of the patients were on a treat and extend regimen. Indeed, the patients did not experience long-term improvement in vision after the switch to aflibercept despite improvement in macular thickness from 536 to 279 $\mu$m at the end of the follow-up. We believe that a contributing factor for the poor functional outcome may be the disease itself. According to Bhisitkul *et al*[3] there is a subset of patients who experience reduced visual outcomes compared with early responders, and we think that the patients in our study may belong to this group. Similar trends in visual outcomes have been reported in patients with wet AMD who were similarly switched to aflibercept.[5,6]

### Conflict of interest

The authors declare no conflict of interest.

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**Sir,**
**Is intraocular pressure the only important postoperative variable? The role of first day postoperative review after vitrectomy**

We read with interest the article published by Alexander *et al*[1] assessing the necessity of day-1 postoperative review of patients undergoing pars plana vitrectomy (PPV). We have certain observations to make. All patients in this study have been given prophylactic antiglaucoma medications (AGMs). These do reduce the intraocular pressure (IOP) spike postoperatively[2] but, conversely, they can mask the true cause of postoperative hypotony. The cause of hypotony in the cases where AGMs were stopped has not been described. Depending on that, management can vary from intensive topical steroids to re-surgery, which is a change in routine treatment.[3] Thus, the empirical use of AGMs and their subsequent cessation without investigating the true cause for hypotony is questionable.

Second, the rate of intervention is unassociated with the indication of surgery in this study. It is obvious that a complex and challenging case would be expected to develop a higher rate of intraoperative and postoperative complications. A larger study sample and subgroup analysis of the indications of surgery should give more meaningful results.

Finally, the entire article seems to center on postoperative IOP management. There are complications like corneal epithelial defects, fibrin membrane, postoperative vitreous hemorrhage, silicone oil in the anterior chamber, postoperative emesis, and most importantly, infection,[4] to name a few, which require either deviation from the routine management or additional and extensive postoperative counseling. Also, what are the medico-legal implications of omitting day 1 review in case a sight threatening complication develops? Though the authors have addressed these issues in the discussion, the