**Sir,
Intravitreal aflibercept for choroidal neovascularisation
in angioid streaks**

We appreciate the interest demonstrated by Tetikoglu *et al*¹ in our publication regarding the use of intravitreal aflibercept as primary treatment for choroidal neovascularisation (CNV) in angioid streaks (AS).²

Currently, anti-vascular endothelial growth factor (VEGF) drugs are the treatment of choice for AS-associated CNV and in this setting, aflibercept is regarded with interest as it has a higher affinity for VEGF-A, as well as the ability to bind VEGF-B and placental growth factor.² Therefore, it is perfectly reasonable to observe patients refractory to bevacizumab¹ and ranibizumab³ to be switched to aflibercept therapy, in alignment with what has been observed in other macular diseases, such as neovascular age-related macular degeneration.⁴

In addition, we agree with Tetikoglu *et al*¹ that the recurrence time of the AS-associated CNV is not just depended on the drug used. Recurrence seems to be a multifactorial event difficult to predict, with some patients needing repeated injections, while others can be activity-free for several years or even develop new CNV lesions.^{3,5} Nevertheless, these case reports^{1–3} suggest that aflibercept is a valid effective option to be considered.

Conflict of interest

Dr SVP has received consultant fees from Bayer and Novartis and has received travel grants from Bayer, Novartis, Alcon, Allergan and Alimera Sciences. Dr LC has received travel grants from Bayer. Dr GDS has received travel grants from Bayer and Heidelberg Engineering. The remaining author declares no conflict of interest.

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Eye (2016) **30**, 896; doi:10.1038/eye.2016.34;
published online 4 March 2016

**Sir,
Comment on: 'Long-term outcomes of neovascular
glaucoma treated with and without intravitreal
bevacizumab'**

In their retrospective study Olmos *et al*¹ compared the long-term outcomes of neovascular glaucoma (NVG) treated with and without intravitreal bevacizumab (IVB; Avastin; Genentech Inc., San Francisco, CA, USA) injections in a large-case comparison study. The authors concluded that vision and intraocular pressure (IOP) in the eyes with NVG treated with bevacizumab showed no long-term differences when compared with eyes that were not treated with bevacizumab. We would like to address some issues regarding the bevacizumab treatment in patients with central/hemicentral retinal vein occlusions (central/hemi-CRVOs)-related NVG.

The assertion made by Olson *et al*¹ that bevacizumab only delays the need for glaucoma drainage implant surgery, serving as an effective temporizing rather than a definitive treatment, is valid only for the fully developed form of NVG (angle-closure glaucoma stage²). However, treatment with IVB injections is a very useful intervention in the early stages of NVG, that is, the prerubeotic, preglaucomatous (rubeosis iridis), and early open-angle glaucoma stages of NVG,² for prevention or even cure of NVG³ by ablation of the ischemic drive for new vessel formation. We demonstrated, for the first time,³ that the prevention of NVG may be enhanced in patients with central/hemi-CRVOs by IVB injections administered as early as possible after the onset of occlusion. Specifically, we prospectively evaluated the cumulative prevalence of NVG in patients with acute (≤ 1 month after the occlusion was diagnosed) central/hemi-CRVOs treated with IVB injections.^{3,4} The treatment consisted of four consecutive IVB injections given off-label in a dose of 2.5 mg per injection ~ 45 days apart followed by *pro re nata* administration over a period of 3 years. No adverse effects or ocular toxicity, including clinically evident sterile or infectious endophthalmitis, IOP increase, retinal ruptures, retinal detachment, and systemic thromboembolic events were encountered during the study. The cumulative prevalence of NVG was 4.08%, a value significantly different from that existing in patients with untreated acute CRVOs (28.5%).⁵

Another aspect of NVG prevention is represented by treating the patients with central/hemi-CRVOs in whom ocular neovascularization already has appeared but IOP still remains within normal limits (eg, the preglaucomatous stage of NVG²). In such cases we administer IVB injections, topical steroids, and cycloplegics; unless the neovascularization subsides with these treatments, we promptly apply panretinal photocoagulation that may prevent or delay any developing of the intractable sight-threatening NVG.

In conclusion, we believe that at a dose of 2.5 mg injected promptly before occurrence of neovascularization and IOP elevation, IVB offers a real benefit and promise for the prevention of NVG in patients with acute central/hemi-CRVOs. Early diagnosis and treatment with bevacizumab are required in order to maintain a good visual status and a satisfactory IOP control.

Conflict of interest

The authors declare no conflict of interest.

Author contributions

Both authors (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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Eye (2016) **30**, 896–897; doi:10.1038/eye.2016.31;
published online 4 March 2016

Sir, Reply to 'Comment on: Long-term outcomes of neovascular glaucoma treated with and without intravitreal bevacizumab'

We thank Călugăru and Călugăru¹ for their constructive comments regarding our article 'Long-term outcomes of neovascular glaucoma treated with and without intravitreal bevacizumab'.² We appreciate their thoughts and their previous work on this topic.

In your letter, you have suggested our conclusion that bevacizumab acts only as a temporizing rather than a definitive treatment for neovascular glaucoma (NVG) is only valid in the fully developed (ie, complete angle closure glaucoma) stage of NVG. However, the large number of patients enrolled in our study represented all stages of NVG, including open angle and angle closure forms of NVG, although documentation of gonioscopy did not allow for sufficient analysis of the effect of bevacizumab on progressive angle closure in NVG.

With regards to central retinal vein occlusion, in the Central Vein Occlusion Study, the application of panretinal photocoagulation (PRP) before the development of any neovascularization of the iris (NVI) failed to demonstrate a statistically significant reduction in the incidence of NVI.^{3,4} Although CVOS recommends waiting for the development of 2 clock hours of NVI as demonstrated by gonioscopic examination, current practice patterns, however, entail performing PRP upon the first evidence of NVI. In addition, our report focused on the treatment of patients who have already developed NVG (defined as intraocular pressure (IOP) > 21 mm Hg associated with NVI and/or neovascularization of anterior chamber angle), rather than prophylaxis to prevent NVG in patients with predisposing conditions, as was the case in your study.

Recently published results from the Diabetic Retinopathy Clinical Research Network Protocol S evaluated visual acuity outcomes in patients with proliferative diabetic retinopathy (PDR) treated with intravitreal ranibizumab compared with PRP over 2 years.⁵ Intravitreal bevacizumab and ranibizumab are used interchangeably by many clinicians. The study demonstrated non-inferiority of repeatedly dosed intravitreal ranibizumab as compared with PRP. However, these results have yet to change practice patterns in PDR management, which involve PRP to eliminate the ischemic drive and induce regression of neovessels, given that in a clinical setting, a monthly injection dosing and/or monitoring schedule is impractical and costly. Loss to follow up could result in risk of vision loss from PDR and possibly NVG. In our opinion, the benefits of timely PRP outweigh the risks attributed to PRP, including peripheral field loss.

As discussed in our article, the effect of intravitreal bevacizumab (IVB) is temporary, and has been associated with recurrence of neovascularization due to its limited duration of action.^{6–9} In a previous paper published by our group and entitled 'Outcomes of treatment of neovascular glaucoma with intravitreal bevacizumab', Kaplan–Meier analysis in Figure 3¹⁰ revealed a linear increase in the cumulative proportion of NVG eyes