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**Sir,**  
**Patterns of ranibizumab and aflibercept treatment of central retinal vein occlusion in routine clinical practice in the USA**

In their retrospective study, Lotery and Regnier<sup>1</sup> comprehensively assessed the real world usage of intravitreal ranibizumab (Lucentis, Genentech, Inc., South San Francisco, CA, USA) and aflibercept (Eylea, Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA) in the treatment of central retinal vein occlusion (CRVO) in the USA. The authors evaluated for the first time the treatment patterns of both drugs in a US claims database for treatment-naïve patients with at least a 12-month follow-up. The mean number of injections received by patients treated with ranibizumab and aflibercept was  $4.4 \pm 2.8$  and  $4.7 \pm 2.9$  ( $P = 0.38$ ), respectively, and the mean interval between injections was 55.1 days and 54.2 days ( $P = 0.44$ ), respectively.

The level 1 evidence of clinical trials<sup>2–4</sup> recommended an aggressive therapy in the first year of treatment, that is, ranibizumab and aflibercept should be given monthly for the first 6 months, with a subsequent 6 months dosing as required (pro re nata (PRN)). The Lotery and Regnier results<sup>1</sup> exhibited that in routine clinical practice in the USA, the number of injections was too small (approximately half of the standard claimed by the clinical trials),<sup>2–4</sup> and the interval between injections was too long. For this reason, we concluded that in the real world, CRVO patients had been insufficiently treated in a period of time in which the amount of vascular endothelial growth factor had been upregulated, which adversely influenced the final restoration of visual function. With such treatment patterns, maximal treatment benefit could not be achieved. We wonder if the data extracted from the US claims database, indeed, reflect the real world results of CRVO patients treated with ranibizumab and aflibercept.

In conclusion, during the first 12 months of treatment, CRVO associated with macular edema should be aggressively treated and the therapy should be applied as soon as possible after CRVO onset. The sooner the treatment is started, the sooner the patient is likely to have gains in visual functions.<sup>5</sup> Of note, PRN treatment undertaken after the first 12 months of aggressive treatment does not prevent the delayed occurrence of deterioration in visual acuity and foveal thickness, which has been reported by all the clinical trials.<sup>2–4</sup>

**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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**Sir,**  
**Response to ‘Patterns of ranibizumab and aflibercept treatment of central retinal vein occlusion in routine clinical practice in the USA’**

We are grateful that Dan and Mihai Călugăru<sup>1</sup> took interest in our article and opened the debate on the optimal level of anti-VEGF in the treatment of central retinal vein occlusion. Our analysis aimed at understanding the real-world treatment patterns of aflibercept and ranibizumab in the United States. We agree with Dan and Mihai Călugăru that the observed treatment patterns in our analysis should not be interpreted as the optimal treatment frequency. In fact, in our conclusions, we recommend conducting further studies to link our findings to visual outcomes that were not available in the claims database at our disposal. The analysis of electronic medical records, similar to the study conducted by the UK Age-Related Macular Degeneration EMR Users