manuscript, our study was retrospective and non-randomized, the absence of a primary IOL implantation at the initial surgery may be a marker for microphthalmia or an overall less developed eye. Thus, the poorer visual outcome may not be related to the aphakia itself, but to the type of eyes left aphakic.[1] The aphakic infants will suffer from the higher risk of secondary glaucoma but this is attributed to selection bias. We have reported that patients undergoing cataract surgery at an early age are at a high risk for the development of glaucoma with or without an IOL implant.[2] Five-year results of the IATS study concluded that younger age at surgery increased the risk for developing glaucoma but the risk was not altered by the choice of aphakia or IOL implantation.[3]

Finally, being a retrospective study, it was difficult to put type of cataract as a predictor. As the purpose of our study was to evaluate preoperative factors influencing visual outcome, we did not include postoperative glaucoma as one of the variables in the model.[1]

Conflict of interest

The authors declare no conflict of interest.

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ME Wilson and RH Trivedi

Storm Eye Institute, Medical University of South Carolina, Charleston, SC, USA
E-mail: wilsonme@musc.edu

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Sir,
Treatment patterns of ranibizumab intravitreal injection and dexamethasone intravitreal implant for retinal vein occlusion in the USA

The article by Nghiem-Buffet *et al*[1] evaluated ophthalmology and treatment visits for ranibizumab (Lucentis; Genentech, Inc., South San Francisco, CA, USA) and dexamethasone (Ozurdex; Allergan, Irvine, CA, USA) in treating naive patients with macular oedema (MO) secondary to retinal vein occlusion in the routine clinical practice in the USA using US patient-level medical claims data.

We would like to address the great discrepancy compared to the current standards regarding the number of treatment visits with ranibizumab and dexamethasone in patients with MO resulting from central retinal vein occlusion (CRVO). A number of 4.1 ranibizumab injections and 1.8 dexamethasone implant injections within a period of 12 months represents approximately half of the standard claimed by the pivotal studies and the current recommendations, and indicates that patients have been insufficiently treated. Thus, the standard injection scheme during the first year of intravitreal ranibizumab therapy for MO owing to CRVO was clearly set by the level 1 evidence of the Cruise study,[2] that is, ranibizumab should be given monthly for the first 6 months, with a subsequent 6-months dosing, as required. The current valid recommendations[3] consider that the duration of $\geq$3-line improvement after dexamethasone implant is typically 2–3 months and that the reinjections generally will be performed after 4–5 months. Similarly, the study by Callanan *et al*[4] demonstrated that treatment with dexamethasone implant every 5 months improved the final outcomes in patients with diabetic MO and met the *a priori* criteria for noninferiority to ranibizumab in average change from baseline visual acuity over 12 months. Noninferiority was achieved with an average of 2.85 dexamethasone implant injections and 8.70 ranibizumab injections.

Altogether, regardless of the intravitreal pharmacotherapy chosen, for example, specific (ranibizumab) or nonspecific (dexamethasone implant) anti-vascular endothelial growth factor (VEGF) agents, the efficacy of treatment depends primarily on the precociousness of the therapy after CRVO onset. Therefore, therapy with anti-angiogenic agents has to be promptly applied as soon as possible after the CRVO onset. Every delay of therapy adversely influences the deterioration of visual functions, which is difficult to restore even with subsequent treatment.[5] Both groups of anti-VEGF substances provide similar rates of vision improvement but with superior anatomic outcomes and fewer injections in the dexamethasone implant-treated eyes. However, more patients receiving the dexamethasone implant lose vision mainly due to cataract.

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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D Călugăru and M Călugăru

Department of Ophthalmology, University of Medicine Cluj-Napoca/Romania, Cluj-Napoca, Romania
E-mail: mihai.calugaru@mail.dntcj.ro

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Sir,
Response to Comment on: Treatment patterns of ranibizumab intravitreal injection and dexamethasone intravitreal implant for retinal vein occlusion in the USA

We are grateful that Dan and Mihai Călugăru[1] took interest in our article. The subject of optimal intensity of anti-VEGF treatment has been discussed previously following the publication of a similar claims data study, which described real-world treatment patterns of ranibizumab and aflibercept for macular oedema secondary to central retinal vein occlusion.[2–4] Our study aimed to understand whether the frequency of ophthalmology visits for patients treated with ranibizumab (Lucentis) and dexamethasone implant (Ozurdex) differed in routine clinical practice in the United States for the treatment of macular oedema secondary to retinal vein occlusion (RVO).[5] Comparing treatment frequency was a secondary objective in our study, with the resulting estimate of ranibizumab treatment frequency being consistent with that previously observed by Lotery and Regnier.[2]

We agree with Dan and Mihai Călugăru that the observed treatment patterns in our analysis should not be interpreted as the optimal treatment frequency. The frequency of treatment administration neither reflects the treatment frequency observed in clinical trials[6,7] nor provides data on visual acuity outcomes attained by the treated cohort. In our discussion, we outline the limitation that visual acuity data were not available in the claims database at our disposal for the conduct of this study.[5]

The Callanan *et al*. study aimed to demonstrate the non-inferiority of dexamethasone implant compared to ranibizumab with respect to mean average change from baseline best-corrected visual acuity (BCVA) over 12 months in patients with diabetic macular oedema. The primary outcome of non-inferiority between treatments was met; however, statistically significant and clinically meaningful differences were observed in mean change from baseline in BCVA favouring ranibizumab. Furthermore, a saw-tooth pattern in central retinal thickness (CRT), indicative of frequent fluctuation of CRT, was observed in the dexamethasone arm. This is in contrast to the sustained improvements in CRT for ranibizumab-treated eyes during the study period.[8] Superiority of dexamethasone implant *vs* ranibizumab in anatomical outcomes was not demonstrated in the Callanan study. Moreover, the authors did not find the claim of superior anatomical outcomes associated with dexamethasone implant adequately supported by randomised clinical trial evidence.[1]

Studies linking treatment patterns to real-world clinical outcomes in RVO will be an important part of understanding outcomes attained by patients in routine clinical practice.

Conflict of interest

SN-B and SB are consultants for Allergan, Bayer and Novartis. SR is an employee of Novartis Pharma AG, Basel, Switzerland. A Skelly is an employee of Novartis Pharma AG, Basel, Switzerland. NY was an employee of IMS Health, London, UK, at the time of the original study, funded by Novartis to perform the statistical analyses for the study, but was not involved in the collection of the dataset or in gaining access to it for the purposes of the study. A Sodi is a member of the Novartis RVO advisory board.

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