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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[1] 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-naive 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 ± 2.8 and 4.7 ± 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[2–4] 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[1] 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),[2–4] 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.[5] 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.[2–4]

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[1] 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

Group, and the analysis of the LUMINOUS observational data will be an important contribution to the debate.[2,3]

Conflict of interest

Andrew Lotery has attended scientific advisory boards and received educational grants from Novartis Pharma AG, Basel, Switzerland and Bayer HealthCare AG, Leverkusen, Germany. Stephane Regnier is an employee of, and owns shares in, Novartis Pharma AG, Basel, Switzerland.

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Sir,
New antithrombotic agents and the need for updated ophthalmic surgery guidelines

Since the publication of the Royal College of Ophthalmologists' Cataract Surgery Guidelines in 2010,[1] several new antithrombotic agents have been introduced into clinical practice that have significant impact on perioperative management and surgical outcomes. These agents are currently frequently missed during pre-assessment as healthcare professionals lack knowledge of their generic as well as trade names. This could potentially lead to a precarious situation where surgery proceeds on a patient taking anticoagulant or antiplatelet therapy, which has not been appropriately managed with potential significant consequences. We feel there is a need for the Royal College of Ophthalmologists to update the published guidelines on cataract surgery incorporating the new antithrombotic agents. There also needs to be published guidelines for other ophthalmological procedures with a view to appropriately manage antithrombotic therapy. We believe that all healthcare professionals involved in pre-assessment of ophthalmic surgery should be made aware of these agents, trade names, and mechanism of action to appropriately and safely manage patients.

The following is a quick list of frequently missed medications to look out for:

- Antiplatelet agents: Prasugrel (Efient) and Ticagrelor (Brilique).
- Anti-thrombin inhibitor: Dabigatran (Pradaxa).
- Anti-factor Xa inhibitors: Rivaroxaban (Xarelto) and Apixaban (Elliquis).
- Vitamin K antagonists: Acenocoumarol (Sinthrome) and Phenindione.

We believe that the lack of awareness of these agents during pre-assessment can lead to avoidable and potentially sight threatening complications. The newer antithrombotic agents should be screened for along with other anticoagulants and antiplatelet agents that are better known and mentioned in the Cataract Surgery Guidelines.[1] Some of the newer agents require monitoring of renal function to calculate the appropriate duration of withholding preoperatively. Others require bridging therapy with reversible agents. Recent review articles of these newer antithrombotic agents suggest practical strategies for appropriate risk stratification and perioperative management.[2,3] We hope that this correspondence raises awareness of these newer agents and the need to create updated formal guidelines with references to the newer antithrombotic therapies. Everyone involved in listing or assessing patients for ophthalmic surgery should be aware of these newer medications and their potential impact on perioperative management and complications.

Conflict of interest

The authors declare no conflict of interest.

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