Sir,
Comment on 'Transitioning to intravitreal aflibercept following a previous treat-and-extend dosing regimen in neovascular age-related macular degeneration: 24-month results'

We read with interest the article by Homer *et al.*[1] We would like to make some statistical and clinical observations.

The subset of eyes included received an average of 23.8 ± 18.8 injections of ranibizumab or bevacizumab over a period of 28 ± 20.5 months. In view of such a large standard deviation, it would have been more accurate to mention the median for the above two values. The mean interval between aflibercept injections was noted to be 59.3 days and that between ranibizumab/bevacizumab was noted as 37 ± 6.1 days. Without the mention of standard deviation for aflibercept, it is difficult to gauge a statistical comparison between the two groups as one cannot ascertain whether the distribution of the intervals for the aflibercept group was parametric or non-parametric. Without that information, application of the *t*-test may not be appropriate.

The inclusion criteria at IRB approval mentions cases with ≥ 6 prior intravitreal ranibizumab/bevacizumab injections. But further in the article, the range of prior injections given mentions 4–62 injections. Whether the pathology can be termed as recalcitrant enough to change the intravitreal agent after just 4 injections is little questionable as past literature shows fairly good long-term response to PRN basis injection of ranibizumab over 1–2 years.[2,3] The treatment protocol for aflibercept followed in this study seems to be 2-monthly injections after the three loading dose injections as authors mention a treatment at a fixed interval of 8 weeks. With that perspective, the fact that the minimum exudation-free period noted was 35 days, it is unclear whether any patient was given repeat aflibercept before 8 weeks.

We would appreciate if the authors could clear the above doubts.

Conflict of interest

The author declares no conflict of interest.

References

1 Homer N, Grewal DS, Mirza RG, Lyon AT, Gill MK. Transitioning to intravitreal aflibercept following a previous treat-and-extend dosing regimen in neovascular age-related macular degeneration: 24 month results. *Eye* 2015; **29**: 1152–1155.
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Sir,
Response to: 'Comment on Transitioning to intravitreal aflibercept following a previous treat-and-extend dosing regimen in neovascular age-related macular degeneration: 24-month results'

We thank Dr Dave for his valuable comments and suggestions and appreciate his interest in our manuscript.[1] We agree with the author that it would be appropriate to also provide the median value for the number of prior injections and duration of treatment, in addition to the standard deviation. The study included patients who had received 23.8 ± 18.8 (median 21.5) prior ranibizumab or bevacizumab injections over the previous 28 ± 20.5 (median 24) months.

We agree with the author that an assessment of the normality of data is a prerequisite for several statistical tests because normal data is an underlying assumption in parametric testing. The quantitative variables for the treatment interval between the two groups were examined by the Shapiro–Wilk test to determine the distribution, which was found to be normal. Because data was normally distributed, the paired test was used. The mean interval between aflibercept injections was 59.3 ± 7.6 days and that between ranibizumab/bevacizumab was 37 ± 6.1 days.

We also agree that 4 injections are insufficient to label a patient as recalcitrant. Our study looked at eyes with ≥ 6 prior intravitreal ranibizumab and or bevacizumab injections. We apologize for typographical error incorrectly mentioning the range, which should read 6–62 injections.

The treatment protocol followed in this study was 3-monthly aflibercept injections followed by treatment at a generally fixed interval of 8 weeks, further extended by 2-week intervals at the discretion of the treating physician based on persistent/recurrent intraretinal fluid (IRF)/subretinal fluid (SRF)/sub-retinal pigment epithelium (RPE) fluid, new hemorrhage/SRF/IRF on exam, increase in central subfoveal thickness (CFT) $>100\,\mu$m and worsening vision by >1 Snellen line. However, as this was a retrospective study, treatment decisions were not absolutely standardized. The range of interval between aflibercept injections was 35–133 days as mentioned in the abstract. There was a single patient who was administered a repeat intravitreal aflibercept injection at 35 days (ie, before 8 weeks).

We appreciate the author's comments and insight into our study. Given the burden imposed by monthly anti-VEGF treatment and the compounded risk of potential adverse ocular and systemic events, conversion to aflibercept offers an approach to increase treatment

interval until such time that long-term drug delivery implants are available. Future, prospective studies with a larger sample size are required to confirm the findings of our initial study and also to potentially identify anatomical characteristics that would be predictive of eyes that might require fewer injections.

Conflict of interest

The authors declare no conflict of interest.

Reference

1 Homer N, Grewal DS, Mirza RG, Lyon AT, Gill MK. Transitioning to intravitreal aflibercept following a previous treat-and-extend dosing regimen in neovascular age-related macular degeneration: 24-month results. *Eye* 2015; **29**: 1152–1155.

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Sir,
Comment on 'The Royal College of Ophthalmologists Guidelines on retinal vein occlusions'

I read with great interest the recently updated retinal vein occlusion (RVO) guidelines published by The Royal College of Ophthalmologists.[1] Ever since the previous guidelines published in 2010 the treatment of RVO in the UK has undergone a rapid evolution, mainly attributed to the recommendation and approval of the use of ranibizumab (Lucentis, Novartis, Basel, Switzerland) and aflibercept (Eylea, Bayer, Berlin, Germany) by The National Institute for Health and Care Excellence (NICE).[2,3] The authors have produced a very clear and comprehensive strategy in stratifying the management plan based on the types of RVO (central *vs* branch and ischaemic *vs* non-ischaemic), the visual acuity (>6/12 *vs* 6/12–6/96 *vs* <6/96), and the presence of macular ischaemia in branch RVO.

However, I believe there is a very slight error in the section on 'anti-vascular endothelial growth factor agents for treatment of macular oedema due to RVO'. The authors quoted NICE TA238 in relation to the use of ranibizumab for treating macular oedema secondary to RVO. NICE TA238 refers to the use of tocilizumab for the treatment of systemic juvenile idiopathic arthritis.[4] This should be replaced by NICE TA283, which refers to the use of ranibizumab for treating visual impairment caused by macular oedema secondary to RVO.[2]

In summary, I would like to thank and congratulate the authors on updating the RVO guidelines with the most current evidence, which helps to streamline the current practice in the UK and ultimately benefits the patients whom we are treating.

Conflict of interest

The authors declare no conflict of interest.

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Sir,
Comment on 'The Royal College of Ophthalmologists Guidelines on retinal vein occlusions: executive summary'

We read with great interest the legitimate and comprehensive guidelines on retinal vein occlusions (RVO) elaborated by Sivaprasad *et al.*[1] However, the reference data were not updated with the available long-term results of the trials, which had dealt with the efficacy of therapy with ranibizumab (Lucentis, Genentech, Inc., South San Francisco, CA, USA) and aflibercept (Eylea, Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA) for macular edema secondary to central RVO (CRVO).[2–4] Specifically, the rates of unresolved macular edema were 56% in the RETAIN study,[2] 65.7% in the COPERNICUS study,[3] and 39.4% in the GALILEO study,[4] after 51.4, 24, and 18 months of follow-up, respectively. Delayed deterioration in the outcome measures in the mentioned trials could be explained by the lower frequency of injections as well as the long duration of time from CRVO diagnosis to initiation of treatment, during which time patients went without treatment for example, an average of 6.39, 2.73,