INTRODUCTION

We would like to address several challenges that have arisen from the study by Larsen et al. (2018), which can be specifically summarized below. There was a selection bias attributable to inclusion in the study of patients with 2 forms of central retinal vein occlusions (CRVO) (with and without macular ischemia) having totally different clinical evolutions and prognoses. Likewise, 2 completely different etiologic subgroups of patients were encompassed, for example, patients older than 50 years who usually have common systemic conditions, such as hypertension and diabetes, and patients less than 50 years, where other mechanisms, such as the hyperviscosity syndrome or inflammatory condition should be specifically considered. In addition, the patients could receive alternative treatment at the investigator’s discretion if visual acuity did not improve after the first 3 mandatory injections and panretinal laser photocoagulation was permitted later than month 3. Taken together, these findings may have confounded the results. The authors documented that patients with lower baseline best-corrected visual acuity (BCVA) exhibited larger mean visual gains at month 24 than did those with higher baseline BCVA. In 2015, we substantiated, for the first time, the impact of initial BCVA on bevacizumab (Avastin, Genentech, Inc., San Francisco, CA) treatment outcomes in patients with macular edema resulting from acute central/hemiscentral retinal vein occlusion (central/hemiscentral RVO) (Călugăru et al. 2015). At month 36, there was an increase in BCVA of 17.5 Early Treatment Diabetic Retinopathy Study (ETDRS) letters (from 48.6 to 65.75 letters) in nonischemic forms and 26.81 ETDRS letters (from 7.6 to 34.41 letters) in patients with ischemic occlusions. The assumption according to which patients with poor initial BCVA may benefit most from anti-VEGF suppression and vice versa, seems to be a somewhat paradoxical and counter-intuitive finding because patients with poor initial BCVA usually have advanced lesions which are difficult to be recovered. And yet, this assertion is logical because patients with low initial BCVA have a larger range of the interval in which visual acuity can be improved in comparison with patients having a better initial BCVA at the time of treatment with a more narrow interval and with small possibilities for improving (treatment “ceiling effect” as a consequence of the limited potential for improvement). The comparison with the Cruise study (Campochiaro et al.2011) was inappropriate because there were completely different proportions of patients with nonperfused retinal status in the two studies, namely, 1.5% in the Cruise study and 15.1% ischemic perfusion type (30% macular ischemia and 38.7% patients with macular ischemia which could not be assessed because of severe intraretinal hemorrhage) in the Crystal study. In addition, the treatment posology for CRVO was deviated from the posology of the pivotal Cruise trial. Nothing was stated regarding our
prospective clinical study (Călugăru et al. 2015) on the 3-year results of bevacizumab treatment in patients with acute (≤ 1 month after the occlusion was diagnosed) central/hemicentral RVOs. Of these patients 50% had ischemic forms of occlusion. This was the first study to report evidence suggesting that early treatment applied immediately after the clinical onset of venous occlusion provided significant and sustained improvements in BCVA and central foveal thickness with inactive disease in most phakic patients with acute central/hemicentral RVOs, making this treatment option a rational and viable therapeutic strategy. The Crystal study (Larsen et al. 2018) demonstrated that the burden of frequent intravitreal injections could be reduced and the longer intervals with improved BCVA could be provided with an individualized dosing regimen of ranibizumab (Lucentis, Genentech) driven by BCVA stabilization criteria. However, the central subfield thickness stabilization criteria are missing from this algorithm. Importantly, we achieved these two goals by increasing the dose of bevacizumab at 2.5 mg (0.1 ml) (Călugăru et al. 2016). Specifically, the treatment initially consisted of 4 consecutive intravitreal bevacizumab injections, each injection given approximately 45 days apart. Thereafter, the therapy was flexible, and subsequent injections were administered on the pro re nata (PRN) basis until dry retina and stable BCVA lasting ≥ 6 months were achieved. The total number of injections of bevacizumab administered in a period of 36 months was 9.14. There were no events of endophthalmitis, retinal tears, or retinal detachment and no serious non-ocular adverse events. Bevacizumab was more effective in patients with ischemic occlusions who required a significantly higher number of injections than did the nonischemic forms (a mean of 9.7 and 8.7 injections, respectively).

Altogether, regardless of the antiangiogenic agents chosen (e.g., bevacizumab/ranibizumab), the treatment paradigms used (e.g., treat-and-extend/PRN/fixed-interval/escalated algorithm), the patient age, the baseline BCVA, and the form of CRVO (ischemic/nonischemic occlusion), the efficacy of treatment depends primarily on the promptness of the therapy after the onset of the retinal vein occlusion (Călugăru et al. 2015, 2016, 2017).

REFERENCES


