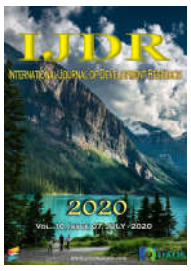
ISSN: 2230-9926

Available online at http://www.journalijdr.com

IJDR

International Journal of Development Research
Vol. 10, Issue, 07, pp. 38629-38630, July, 2020
https://doi.org/10.37118/ijdr.19556.07.2020



RESEARCH ARTICLE OPEN ACCESS

COMPARING THE EFFICACY OF BEVACIZUMAB AND RANIBIZUMAB IN PATIENTS WITH RETINAL VEIN OCCLUSION

Dan Călugăru and *Mihai Călugăru

Department of Ophthalmology, University of Medicine Cluj-Napoca/Romania

ARTICLE INFO

Article History:
Received 29th April, 2020
Received in revised form
07th May, 2020
Accepted 27th June, 2020
Published online 30th July, 2020

Key Words:

Bevacizumab; Ranibizumab; Retinal vein Occlusion; Best-Corrected Visual Acuity.

Corresponding author:
Mihai Călugăru

ABSTRACT

The authors are commenting on the study entitled **:**"Comparing the efficacy of bevacizumab and ranibizumab in patients with retinal vein occlusion" published by Vader et al. in Ophthalmology Retina 2020;4(6):576-587,which compared the efficacy of intravitreal injections of bevacizumab to ranibizumab in the treatment of retinal vein occlusion– emergent macular edema. The study found that best-corrected visual acuity gain, anatomic outcomes, and safety were remarkably equivalent at 6 months in both treatment arms. However, the validation, extrapolation, and generalizability of the authors' conclusions can be made only by statistical analyses including all the missing baseline factors mentioned by us in addition to the baseline characteristics already evaluated in this study.

Citation: ***Dan Călugăru and Mihai Călugăru. 2020*** "Comparing the efficacy of bevacizumab and ranibizumab in patients with retinal vein occlusion*", International Journal of Development Research*, 10, (07), 38629-38630.

INTRODUCTION

We read with interest the study by Vader *et al.* (2020) which compared the efficacy of intravitreal injections of bevacizumab (Avastin; Genentech, Inc., San Francisco, CA, USA) to ranibizumab (Lucentis; Genentech, Inc.) in the treatment of retinal vein occlusion (RVO) – emergent macular edema (ME). Based on the change in best corrected visual acuity (BCVA), the study revealed that bevacizumab is noninferior to ranibizumab for patients with ME following RVO when receiving monthly injections for a period of 6 months. Likewise, anatomic and safety outcomes did not differ between treatment groups. We would like to address several challenges that have arisen from this study which can be specifically summarized below.

There was a selection bias attributable to inclusion in the study and pooled analysis of patients with 2 forms of RVOs (ischemic and nonischemic occlusions) as well as 2 types of RVOs (branch retinal vein occlusion [BRVO] and central retinal vein occlusion [CRVO]) having totally different pathogeneses, clinical features and evolutions, prognoses, and management. Likewise, 2 completely different etiological subgroups of patients with definitely different prognoses were lumped together, namely, patients older than 50 years who usually have common systemic vascular conditions (hypertension and diabetes), and patients less than 50 years, in whom other mechanisms, such as the hyperviscosity syndrome or inflammatory condition should be specifically considered (Călugăru *et al.* 2019).Of note, the graduation of the intraretinal cysts at presentation and after 6 months was at the discretion of the local investigators at the 8 acclaimed academic and nonacademic centers throughout the Netherlands without confirmation by an external reading center as was the case with establishing the diagnosis of the 3 types of RVOs, namely BRVO, CRVO, and hemicentral retinal vein occlusion (hemi-CRVO). Taken together, these findings may have confounded the results.

The authors included the hemi-CRVO patients in the CRVO subgroup for analysis, although the 2 forms of RVOs, despite their similar pathogenesis, have totally different clinical features and prognoses. Of note, because of a stratification error, some hemi-CRVO patients were randomized also in the BRVO subgroup resulting a mixed BRVO subgroup and causing an inadvertent bias. Inclusion of the hemi-CRVO

patients in the CRVO subgroup may explain the greater improvement in BCVA in this mixed subgroup compared with the mixed BRVO subgroup in contrast with the reverse highlighted by the existing ophthalmic literature where the BCVA gains in BRVO patients exceed those in CRVO patients (Epstein *et al.* 2012; Campochiaro *et al*. 2010; Brown *et al*. 2010).

The authors did not specify the forms of RVOs included (ischemic/nonischemic occlusions). This study is the only randomized trial that does not mention the duration of the symptoms after RVO onset at presentation as well as the perfused retinal status of the RVOs. Considering the pretty good values of the baseline BCVA (< 24 letters < 79) in patients of this study and exclusion of patients with structural damage within 600 µm of the center of the macula (Vader *et al.* 2020), we inferred that most of the patients included experienced nonischemic RVOs, that have a much better prognosis than those with ischemic forms, even without treatment. One argument in support of this assumption is that the authors of this study compared their final outcomes with those of the Cruise (Brown *et al*. 2010) and Swedish (Epstein *et al.* 2012) trials, two studies with well defined perfused retinal status (98.5% and 58.9% nonischemic RVOs, respectively).

The following relevant data, which should have been included in the statistical analyses, are missing from the study: the age stratification of the patients (≥50/<50 years); the existence or otherwise of the disorganization of retinal inner layers and its severity (mild, severe, or severe with damaged ellipsoid zone); the optical coherence tomography (OCT) patterns of the vitreoretinal interface abnormalities (vitreomacular adhesion, full-thickness macular hole, lamellar macular hole, combined epiretinal membrane and vitreomacular traction); the location of the intraretinal cysts on OCT (inner or outer nuclear layers/ganglion cell layer) at presentation and at the completion of the study; the damages of the photoreceptor cell layer (thinning of the outer nuclear layer/external limiting membrane defects, ellipsoid zone disruption/interdigitation zone loss); and the qualitative status of the retinal pigment epithelial band-Bruch membrane complex (pigment migration within the neurosensory retina, retinal pigment epithelium [RPE] porosity, microrips or blowouts in the RPE, focal RPE atrophy, RPE thickening) (Călugăru *et al.* 2019).

In the actual assessment of the final results of this study we considered the currently available assertion that evaluation of the outcomes has to be guided by anatomical measure data with visual changes as a secondary guide (Freund *et al.* 2015). Accordingly, despite the obvious similar improvement of BCVA with 15.3 letters for bevacizumab and 15.5 letters for ranibizumab, the structural data after 6 months of monthly injections were poor. Specifically, the proportion of patients with intraretinal cysts was fairly high in the both treatment groups, being significantly higher in the bevacizumab group (42.5%) compared to ranibizumab group (31.5%). These data certify unresolved ME owing to insufficient deturgescence of the macula and indicate that the disease process is still active and progressive requiring further treatment with antiangiogenic agents. Comparing the differences in OCT outcomes between the bevacizumab and ranibizumab groups with low (≤ 62 letters) and high (≥ 63 letters) baseline BCVA, the authors found a significant difference between the 2 subgroups, because a larger difference was seen in the decrease in central area thickness between bevacizumab and ranibizumab in the patient group with higher initial BCVA (Vader *et al.* 2020). Therefore, the anatomic outcomes of this study were not equivalent at 6 months between treatment arms. Also, the same results from the analysis of the safety of the 2 treatments, namely significantly more patients treated with bevacizumab experienced an adverse event in the MedDRA system organ class General Disorders and Administration Site Conditions including reports of fever, a sore throat, or the flu in between study visits and pain, burning sensations or a hyposphagma after injection.

Altogether, the study found that BCVA gain, anatomic outcomes, and safety were remarkably equivalent at 6 months in both treatment arms. However, the validation, extrapolation, and generalizability of the authors' conclusions can be made only by statistical analyses including all the missing baseline factors mentioned by us in addition to the baseline characteristics already evaluated in this study.

Acknowledgments/disclosure

All authors have completed and submitted the ICMJE form for disclosure of potential conflicts of interest. No financial disclosures. Both authors (D.C and M.C) were involved in the design and conduct of the study; collection, management, analysis and interpretation of the data; and preparation, review or approval of the manuscript. The authors have full control over the primary data and they agree to allow the International Journal of Development Research to review their data if requested.

REFERENCES

Vader MJC, Schauwvlieghe ASME, Verbraak FD, et al. 2020. Comparing the efficacy of bevacizumab and ranibizumab in patients with retinal vein occlusion. *Ophthalmology Retina.,* 4(6):576-587.

Călugăru D, Călugăru M. 2019. Predictors of neovascular glaucoma in central retinal vein occlusion. *Am J Ophthalmol.,* 205(September):200-201.

Epstein DLJ, Algvere PV, von Wendt G, et al. 2012. Bevacizumab for macular edema in central retinal vein occlusion: a prospective, randomized, double-masked clinical study. *Ophthalmology.,* 119(6):1184-1189.

Campochiaro PA, Heier JS, Feiner L. et al., 2010. Ranibizumab for macular edema following branch retinal vein occlusion. Six-month primary end point results of a phase lll study. *Ophthalmology* 117(6):1102-1112.

Brown DM, Campochiaro PA, Singh RP, et al. 2010. Ranibizumab for macular edema following central retinal vein occlusion. Six-month primary end point results of a phase ll study. *Ophthalmology.,* 117(6):1124-1133.

Călugăru D, Călugăru M. Association of disorganization of retinal inner layers with ischemic index and visual acuity in central retinal vein occlusion. *Ophthalmology Retina* 2019;3(1):Page e1

Freund KB, Korobelnik JF, Deveny R, et al. 2015. Treat-and-extend regimens with anti-VEGF agents in retinal diseases. *Retina.,* 35(8):1489-1506.

****