

## Format for ANSWERING REVIEWERS



Feb 21, 2015

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 16150-edited.doc).

**Title:** Approved pharmacotherapy for macular edema secondary to branch retinal vein occlusion: A review of randomized controlled trials in dexamethasone implants, ranibizumab, and aflibercept

**Author:** Jia-Kang Wang

**Name of Journal:** *World Journal of Ophthalmology*

**ESPS Manuscript NO:** 16150

The manuscript has been improved according to the suggestions of reviewers and highlighted the changes of the manuscript with red letters:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

(1) Reviewer 1: Good summary of recent clinical studies addressing BRVO treatments.

No response

(2) Reviewer 2: This manuscript entitled “Clinical outcome of approved pharmacotherapy for macular edema secondary to branch retinal vein occlusion” was to review the treatment for macular edema secondary to branch retinal vein occlusion (BRVO) have approved by FDA of US. This is an interesting and well written. Major comments: 1) Title, I think author miss typing “vein” on branch retinal vein occlusion. 2) I think this is a kind of review paper for the treatment of BRVO, it is better to write clearly about how to select the articles by well randomized controlled trial or in recent 5 years. 3) There are three therapy approved by FDA of US.: Dexamethasone implants, Ranibizumab, and Aflibercept, I think if can have subtitle in manuscript will make it more clearly to read.

Response: Response: I changed the title to “**Approved pharmacotherapy for macular edema secondary to branch retinal vein occlusion: A review of randomized controlled trials in dexamethasone implants, ranibizumab, and aflibercept**” and I added the last sentence of the first paragraph “Herein the clinical outcome of the randomized controlled studies in these approved pharmacotherapies will be reviewed.”

(2) Reviewer 3: The manuscript be Wang et al is a review article specific to macular edema in branch retinal vein occlusion. Some minor improvements can be made to the manuscript. 1) The title should be changed to show the nature of the study ie a review because "clinical outcomes" gives the false impression of a clinical study 2) The authors confirm FDA approval of the treatment modalities but the European Medical Agency approval terms should also be mentioned as the World Journal of Ophthalmology has a broad diffusion 3)the complications of the treatment modalities are not sufficiently addressed: A) frequency of antiVEGF and complications, B ) dexamethasone implants and IOP increase indicationg specific times for

clinical monitoring and C) migration of implant into the anterior chamber in patients with posterior capsule rupture etc. The information can be obtained from the following articles and it would be useful to cite these. Lambiase A et al. An update on intravitreal implants in use for eye disorders. *Drugs of Today* 2014; 50(3):239-249 Khurana RN et al. Dexamethasone implant anterior chamber migration..*Ophthalmology* 2014; 12(1):67

Response:

- A) I changed the title to **“Approved pharmacotherapy for macular edema secondary to branch retinal vein occlusion: A review of randomized controlled trials in dexamethasone implants, ranibizumab, and aflibercept”**
- B) I changed the last sentence of the first paragraph to “The Food and Drug Administration of US and European Medicines Agency have approved intravitreal injections of dexamethasone implants, ranibizumab, and aflibercept for treating macular edema secondary to BRVO. “
- C) I added three sentences on 7<sup>th</sup> sentence of the page 4 “IOP required specific time for clinical monitoring.<sup>15</sup> The dexamethasone implants were reported migration into the anterior chamber, causing permanent corneal edema.<sup>16</sup> Absence of lens capsule and prior vitrectomy were risk factors for Ozurdex anterior migration.<sup>16”</sup> and add reference 15 and 16 “Lambiase A, Abdolrahimzadeh S, Recupero SM. An update on intravitreal implants in use for eye disorders. *Drugs Today (Barc)*. 2014;50:239-49. and Khurana RN, Appa SN, McCannel CA, Elman MJ, Wittenberg SE, Parks DJ, Ahmad S, Yeh S. Dexamethasone implant anterior chamber migration: risk factors, complications, and management strategies. *Ophthalmology* 2014;121:67-71”
- D) I added a new paragraph before the last sentence “Although there was no serious adverse

effect reported in studies of ranibizumab and aflibercept for macular edema secondary to BRVO, some rare serious complications were found after use for other indications. Retinal pigment epithelium tears, macular ischemia, cataract progression, retinal breaks and detachment, endophthalmitis, macular hole, and intraocular inflammation were reported as ocular complications after intravitreal anti-VEGF for treating neovascular AMD.<sup>24</sup> Systemic adverse effects were uncommonly reported such as thromboembolic events (stroke and myocardial infarction) and gastro-intestinal bleeding.<sup>25</sup> and add references 24 and 25 “Wong LJ, Desai RU, Jain A, Feliciano D, Moshfeghi DM, Sanislo SR, et al. Surveillance for potential adverse events associated with the use of intravitreal bevacizumab for retinal and choroidal vascular disease. *Retina* 2008;28:1151–1158 and Comparison of Age-related Macular Degeneration Treatments Trials (CATT) Research Group. Ranibizumab and bevacizumab for treatment of neovascular age-related macular degeneration: two-year results. *Ophthalmology* 2012;119:1388-1398”

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Ophthalmology*

Sincerely yours,

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