

Dear Jin-Lei Wan,

Thank you for your precious time and comments and awfully sorry for the tardy reply. I also need to express my gratitude for the reviewers' perusal of my article and their thoughtful corrections which guided me through my work. The following is what I corrected based on your scholarly comments:

- 1) The word "major" was deleted.
- 2) The second sentence was modified.
- 3) This sentence seemed not to be in our introduction section.
- 4) Four main hypotheses about how hyperglycemia causes diabetic complications were added according to the reviewer comment and a new reference which was suggested by the reviewer was added.
- 5) The word "drug" was added.
- 6) 4.88 days in rabbits.
- 7) We omitted this sentence. This was a highlighted.
- 8) This sentence was revised according to the reviewer's comment.
- 9) Rabbit was added to the sentence.
- 10) RISE and RIDE studies were sure not similar to RESOLVE study in terms of ranibizumab dose. What we meant was the similarity in terms of comparing sham group with ranibizumab group.
- 11) The results of VIVID and VISTA-DME which were presented at EURETNA 2013 were added.
- 12) Since the details and the amount of visual acuity were mentioned in tables, we found it unnecessary to include them in the text.
- 13) Such results have been described in the "Published results of intravitreal corticosteroids for DME" section.
- 14) The reviewer's comment was added in the Published results of intravitreal corticosteroids for DME section.
- 15) Repeated injections of anti-VEGF may cause retinal atrophy in respect of younger age of patients with DME. The development of GA in AMD cases with the use of ranibizumab is just an extrapolation for describing a potential for the development of such a condition in DME cases.
- 16) The risk of endophthalmitis after intravitreal anti-VEGF injections according to the findings of a new article was added.
- 17) The results of the Smiddy study which had evaluated the cost/benefit of treatment of DME were added.
- 18) The sentence was revised and one reference was added. The sentence "The effect of drugs usually decrease over time and therefore the dose and frequency of application should be raised considering the increase in the incidence of adverse events" was removed according to the reviewer's comment.
- 19) The future horizon section was made brief.
- 20) This guideline is according to a new article in AJO titled "Management Paradigms for Diabetic Macular Edema" which was added to references.
- 21) The summary of practical clinical guidelines has been prepared based on the latest publication in AJO "Mitchell P, Wong TY, Diabetic Macular Edema Treatment Guideline

Working G. Management paradigms for diabetic macular edema. Am J Ophthalmol.
2014;157(3):505-13”

22) Abbreviations in the table was changed according to the reviewer’s comment.

23) Some minor studies in the table were removed according to the reviewer’s comment.