Author’s response to reviews

Title: Therapeutic Effects of Ranibizumab in Patients with Polypoidal Choroidal Vasculopathy

Authors:

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Author’s response to reviews:

Technical Comments:

Authors are advised to remove the black frames from the Figure 1 and 2. Response: Black frames removed.

Editor Comments:

Authors should consider addition of representative fundus, indocyanine green angiography and OCT images before and after Ranibizumab monotherapy if available i.e. including best and worst outcomes of the treatment. Response: I added Figure 3 and Figure 4. Figure 3 is a patient with complete polyp regression. Figure 4 is a patient with polyp recurrence. Fundus photography, FFA+ICGA and OCT images at baseline and 12 month follow-up are numbered as ABCDE. Figure legend added at the end of the manuscript (line 428-435, line 437-443, page 22).

Also few sentences in the manuscript that in my opinion can be rephrased and I agree with Dr. Saxena and Dr. Mukwaya that manuscript can benefit from additional editing and proofreading preferably by native speaker or professional editorial services. Response: I will ask professional editorial services for help once this revision is approved by editors.
Background

line 47 "Can anti-VEGF treatment alone manage the disease?" Consider rephrasing as “However, capacity of ranibizumab monotherapy to manage the PCV is not sufficiently explored.” Response: Rephrased (Background, line 66-67, page 3-4).

Line 69-71 Recent academic hotspots have focused on whether to choose combination therapy or anti-VEGF therapy in the initial treatment of PCV. There is no consensus on the optimal treatment plan. Consider rephrasing as “There is currently no consensus on the optimal treatment plan on whether to choose combination therapy or anti-VEGF therapy in the initial treatment of PCV”. Response: Rephrased (Background, line 70-71, page 4).

Methods

Line 79 Please emphasize that written consent was obtained from the patients. Response: Revised (Methods, line 79-80, page 4).

Line 85 Authors encouraged not to use “etc.” in the scientific manuscript. Response: Revised (Methods, line 91-92 page 4).

Line 87 “except uncomplicated cataract extraction with intraocular lens implantation” while it is understandable choice combining patients with and without cataract extraction into single cohort is potential source of heterogeneity that need to be addressed in the discussion. Response: Because of our study is a retrospective study and the age distribution in PCV’s disease population, cataract is a common condition in patients enrolled. We described in methods section that other ocular diseases that could damage visual acuity were excluded and that includes severe cataract. Significant changes in lens opacity were not present during follow-up, therefore we believe enrolling patients with and without cataract extraction will not significantly influence our results. However, we added this potential source of heterogeneity in discussion section (line 278-281, page 15). We also added that no patients required ocular surgery during follow-up (results, line 191-192, page 11).
Reviewer reports:

Sandeep Saxena, M.D, FRCSEd, FRCS, FRCOphth (Reviewer 1): This case series highlights the role of Ranibizumab in PCV.

Trial registration number should not be included in abstract but should either be included in methods or at the end of manuscript text as separate heading, which ever is suitable for the journal. Response: Trial registration number was moved to methods section (methods, line 118-119, page 6).

Few sentences have been repeated in intravitreal technique section. They should be deleted. Response: Repeated sentences deleted (methods, line 99-104, page 5).

Authors should define assessment of ICG-based PCV activity for the readers. Response: Definition was added (methods, line 82-86, page 4).

In discussion authors should add comments how their study adds further to literature in view of existing EVEREST and LAPTOP trials. Response: Comments added (discussion, line 242-245, page 13).

Anthony Mukwaya, Ph.D. (Reviewer 2): Comments to manuscript BOPH-19-00063

1. There are minor grammatical errors which authors should address, for instance in the abstract lines 29-30, authors write letters without an 'l' at the start of the word. Response: Revised (abstract, line 30, page 2). I will ask professional editorial services for help once this revision is approved by editors.

Methods


3. Authors should consider tabulating the number of eyes and the exact treatment(s) they received, to make it easy for the would-be reader to follow. Response: Added as table 2 (results, line 138-139, page 7).
Results

4. In line 128, authors state that 9 eyes received PDT, and another 9 eyes received combination of treatment of both ranibizumab and PDT, however in line 142, authors refer to the all the 18 eyes as those that received additional PDT. This could be misleading given that 9 eyes received combination treatment, and therefore needs to be clarified. Response: Revised as “When 18 eyes which received PDT treatment (9 eyes with additional PDT, and another 9 eyes with combination treatment) was evaluated separately” (results, line 148-149, page 8).

5. Under subheading ‘change in optical coherence tomography’. Please check the abbreviation of micrometers. It should be written as in 'µm' instead of 'µ m'. Response: Revised (results, line 154-157, page 8).

6. Line 155. If authors did not perform indocyanine green angiography at 3 months, is a single time point analysis at 12 months follow up enough to call this a regression rate? Response: The main limitation of our study was its retrospective nonrandomized nature. Not all patients received ICGA at 3 months follow-up therefore polyp regression at 12 months follow-up could possibly be the result of natural course of disease. We added the above in discussion section (line 275-277, page 15).

7. Lines 157-159. Please define 'complete regression', in addition, how did the authors determine the size of polyps, since this is not mentioned anywhere in the methods. Response: Definition was added (methods, line 82-86, line 88-89, page 4-5).

8. Line 165-167. If the BCVA at 12 months follow up was not different from that at baseline as observed by the authors (see lines 138-140), how then do baseline VA, baseline CRT, retinal/subretinal hemorrhage, subretinal fluids and greatest lesion diameter correlate significantly with 'better VA' at final follow-up? Response: Sixteen of 80 eyes had VA improvement of more than 15 letters, 62 eyes had stable vision. We used univariate linear analysis and stepwise multivariate analysis to evaluate the correlation between the baseline characteristics and changes in visual acuity at 12 months follow-up. We found correlation between several baseline characteristics and VA at 12 months follow-up, meaning patients with certain characteristics tend to have relatively better VA than other patients. Our expression was not accurate. We revised the original phrase to “significant and independent factors predictive of relatively better visual acuity” (abstract, line 39, page 2; results, line 182 and 184, page 10).

9. Authors should refer to the figures appropriately in the description of the results, to guide the reader. Response: Figure 1 and figure 2 mentioned in results section (line 146 and 157).

10. Authors should accompany the results in lines 146-154 and 155-161 with an appropriate figures/tables for better visualization of the results. Response: Results shown in table 3 and 4 (results, line 171-176, page 9-10).
11. Figure 1 and 2 legends. Often a single Asterix is used to depict a significant p value, and multiple Asterix to depict the degree of significance. What exactly do the double Asterix represent in this case, as shown by the authors? Response: Single Asterix is for statistical difference (p<0.05), double Asterix is for significant statistical difference (p<0.01). I have added this to figure legends.

12. Figure 2 legend does not correspond to the data shown in figure 2. For example, the legend describes CRT, however, the y-axis of the figure is labeled as BCVA, and the values too seem to represent BCVA and not CRT. Please clarify. Response: I have loaded figure 1 as figure 2 by accident. Figure 2 now corrected.

13. Authors should consider providing the results for both the regression and multivariate analysis in at least tabular format. Response: Results shown in table 5 (results, line 186-188, page 10-11).

Discussion

14. Results of visual outcome. Authors show a return to baseline of BCVA at 12 months follow up, which is interesting and should be discussed, speculating possible explanations for this outcome. Response: we added possible explanations for VA results in discussion (discussion, line 229-233, page 13).