Author’s response to reviews

Title: Indirect comparisons of ranibizumab and dexamethasone in macular oedema secondary to retinal vein occlusion

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Author’s response to reviews: see over
Reviewer's report

**Title:** Indirect comparisons of ranibizumab and dexamethasone in macular oedema secondary to retinal vein occlusion

**Version:** 1  
**Date:** 14 October 2014  
**Reviewer:** Petros Pechlivanoglou

**Reviewer's report:**

The revised version of the manuscript has greatly improved compared to the older version. The assumptions are better laid out and the reporting of the results is now more complete. However, there are in my opinion still a few things that need to be revised. I outline my comments below:

**Major Compulsory Revisions:**

1. I think the conclusions section in the abstract and the discussion/conclusion sections in the manuscript have to be toned down with respect to the relative superiority of ranibizumab. A novel method is being implemented, only a subset of the available data (e.g. no 3 month comparisons and no comparisons where the GENEVA trial is used as baseline are being presented) is used, and the results are not significant using a more classical interpretation. All these point to a very careful interpretation of the findings. Please adjust your interpretation in a way that reflects this uncertainty and also incorporates the findings from the comment below

   - We have drawn specific attention to the wide credible intervals and the classical non-significance of the results. The abstract required some rewording to accomplish this within the 350 word limit and we hope the new version is acceptable.

2. In this version of the manuscript it becomes more apparent that the analysis was conducted to serve a health economics model. However, I believe that it would be beneficial for the reader that is interested purely on the clinical comparison of the two treatments to know what the results of the comparison where a) when the GENEVA trial is used as baseline and b) the comparisons are done at month 3. I think these results have value (especially if they change the interpretation of the findings), should be discussed in the manuscript and should be included at least as an appendix.

   - We have included the comparison on the GENEVA scale and in the GENEVA setting in Tables 9 and 10 and have included this comparison in the discussion. We agree that the comparison at month 3 would have value due to the potential bias in the BRVO comparison (not CRVO, as laser was only offered at month 3 in the BRAVO and not the CRUISE trial). However, we were unable to obtain data for this timepoint. We have included a simple comparison of relative risks of achieving >=15 letters BCVA change at 3 months in the discussion using published evidence on the GENEVA, BRAVO and CRUISE trials. We have added clarification in the manuscript.

3. In the introduction section it is still unclear what the aim of the analysis was. Was it that the authors wanted to a) compare the relative effectiveness of the two treatment options in a rigorous way b) develop a new method to compare such
data and the presented comparison is merely an illustration or 3) estimate the input parameters for a health economic model. Again, the analysis and interpretation should be analogous to the aim set in the introduction section.

- It was (a). Our motivation was to perform the indirect comparison in order to inform a HE model but the comparison of relative effectiveness was our primary goal. We developed a useful methodology along the way but the motivation was always the specific application. We have edited the introduction, discussion and conclusions to clarify that we were originally motivated to inform a health economic model and hope it is now acceptable.

4. what do you mean by consistent comparisons"in line 46? What was your way of defining consistency?Please explain somewhere in the text.

- This was a poor choice of wording on our part. We meant that the comparisons could be conducted on the same category of change in BCVA. We have removed the word consistent to avoid confusion and mentioned at the end of the abstract that we were able to conduct comparisons when events were reported on different categorical scales.

Minor essential Revisions:
1. Line 173 : "Appear to BE similar"
- Changed

Level of interest:An article whose findings are important to those with closely related research interests
Quality of written English:Needs some language corrections before being published
Statistical review:Yes, and I have assessed the statistics in my report.
Declaration of competing interests:
I declare I have no competing interests

Reviewer's report
Title:Indirect comparisons of ranibizumab and dexamethasone in macular oedema secondary to retinal vein occlusion

Version:1 Date:9 October 2014
Reviewer:Andrew Elders

Reviewer's report:
The authors have successfully addressed many of the aspects that were missing from their previous submission, particularly with respect of clearly stating the primary endpoint and the discussion of the methodology.

Major Compulsory Revisions
They also have now included a good description of the literature search, although it’s not completely clear why it was valid to exclude the ROCC trial: all eligible studies should be included in the analysis even if the sample is small.
• We excluded ROCC because it did not report numbers of patients achieving different categories of BCVA change and so could not be included in our indirect comparison. Our point about the sample size was that it was not a great loss of evidence (rather than attempting to justify omitting it) but can see that this was not clear in the original submission. We have clarified this exclusion in the text.

Discretionary Revisions
Outcomes reported at 3 months remain excluded from the study and the investigators should state the reason for this.
• The reason is the lack of data for the 3 month endpoint. We attempted to access this but it was not possible. We have included a simple Bucher indirect comparison using publicly available data on the 3 month endpoint.

Minor Essential Revisions
One minor point to note is that the word “comparator” is missing when the PICOS criteria is mentioned.
• We have corrected this error.

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable
Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests:
I declare that I have no competing interests.