

BMJ - Decision on Manuscript ID BMJ.2018.044227

Body:

11-Sep-2018

Dear Dr. Gyawali

Manuscript ID BMJ.2018.044227 entitled "The toxicity profile was acceptable-acceptable to whom?" which you submitted to BMJ,

Thank you for sending us your revised paper and for your patience while we have been considering it. We think the revisions have much improved the manuscript.

We recognise the paper's potential importance and relevance to general medical readers, but as you'll see from the review from our statistical editor and our comments on the attached version of your manuscript there are several important aspects of the work that still need clarifying.

We hope very much that you will be willing and able to revise your paper as explained in the attached document. We are looking forward to reading the revised version and, we hope, reaching a final positive decision.

Yours sincerely,

Navjoyt Ladher
nladher@bmj.com

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** Comments from the external peer reviewers**

Reviewer: 1

Recommendation:

Comments:

The authors have satisfactorily responded to my comments and suggestions.

Additional Questions:

Please enter your name: Laurent Azoulay

Job Title: Associate Professor

Institution: McGill University

Reimbursement for attending a symposium?: No

A fee for speaking?: No

A fee for organising education?: No

Funds for research?: No

Funds for a member of staff?: No

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Reviewer: 2

Recommendation:

Comments:

I have read the responses of the authors to reviewers and editorial questions which overall appear appropriate but have been unable to access the corrected file.

Additional Questions:

Please enter your name: Jane maher

Job Title: Consultant

Institution: EN herts hospital and Macmillan cancer support

Reimbursement for attending a symposium?: No

A fee for speaking?: No

A fee for organising education?: No

Funds for research?: No

Funds for a member of staff?: No

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Reviewer: 3

Recommendation:

Comments:

This article covers an important topic, but it essentially presents results of a systematic review and meta-analysis, without the required reporting rigour. This seems to go against what the authors are arguing for, i.e. clear and full reporting. I understand that including a detailed description of the methods may not fit with the usual Analysis article format. I can also see that the aim, as the authors state, is not to provide "accurate data on increased risk of toxicities". However, if the authors present analysis and results of this risk, i.e. the section on "By how much is the risk of toxicities higher...", then they are running the risk of providing readers with results that, in their words, may not be accurate. I'm not sure how best to take this forward, because I do sympathise with the argument. However, if these analyses are presented, then the methods really should be reported as they would be in any research study, following reporting guidelines for systematic reviews and meta-analyses. At the moment this is not the case.

As far as the results that are presented go, it is difficult to interpret these. Some of the differences between control and experimental arms may have occurred by chance, and trials would not have been powered to find a difference in AEs between arms – therefore the authors cannot infer that the experimental arms increase toxicities. In fact the confidence intervals for incidence overlap between control and experimental arms, and the same point estimate for FAEs is the same.

Minor points:

I thought that it would have been useful to also include an analysis of those studies that did not downplay toxicities as defined by the authors – this would provide a helpful comparison of the risk of toxicities overall.

Page 5 – studies with no data – why? Was this because there were no severe AEs in these studies? Was this for both arms?

It is not clear how the risk ratios were calculated – particularly 0.89 for the FAEs, when the rate in both control and experimental arms was stated as 1.6%.

Additional Questions:

Please enter your name: Katie Harron

Job Title: Senior lecturer

Institution: UCL

Reimbursement for attending a symposium?: No

A fee for speaking?: No

A fee for organising education?: No

Funds for research?: No

Funds for a member of staff?: No

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The full text online version of your article, if accepted after revision, will be the indexed citable version (full details are at <http://resources.bmj.com/bmj/about-bmj/the-bmjs-publishing-model>).

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11-Sep-2018

File 1:

[gyab044227.1nl.docx](#)