Author's response to reviews

Title: Efficacy and safety of tofacitinib in the treatment of rheumatoid arthritis: a systematic review and meta-analysis

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Version: 2 Date: 6 September 2013

Author's response to reviews: see over
6th September 2013

Professor Timothy Shipley
Executive Editor
BMC Musculoskeletal Disorders
BioMed Central
236 Gray's Inn Road
London WC1X 8HB
United Kingdom

Dear Professor Shipley,

Submission of revised manuscript: "Efficacy and safety of tofacitinib in the treatment of rheumatoid arthritis: a systematic review and meta-analysis".

Thank you very much for the comments. We have read through the comments and have revised the manuscript accordingly. Our response to the reviewers’ comments is attached for your consideration. We thank you for your consideration.

Yours sincerely,

Ian C K Wong

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Author's response to reviews

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Version: 2 Date: 6th September 2013

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

Title: Efficacy and safety of tofacitinib in the treatment of rheumatoid arthritis: a systematic review and meta-analysis

Version: 1 Date: 5 June 2013

Reviewer: Negin Mohtasham

Reviewer’s report:

1. The review should be updated because after the time you have submitted the paper, new systematic reviews relevant to your meta-analysis have been published one of which is following article: Safety profile of protein kinase inhibitors in rheumatoid arthritis: systematic review and meta-analysis. Salgado E, Maneiro JR, Carmona L, Gomez-Reino JJ. Ann Rheum Dis. 2013 Apr 18.

   Thank you for your suggestion and we now update our review by discussing this meta-analysis in the discussion part. Please refer to page 14 line 16-17 and page 15 line 16-18.

2. To reduce the risk of bias, it is much better to consider some other research sources, for this I recommend to study following article: Savoie, Isabelle; Helmer, Diane; Green, Carolyn J.; Kazanjian, Armine (2003). “Beyond Medline: reducing bias through extended systematic review search”. International Journal of Technology Assessment in Health Care 19 (1): 168#78. doi:10.1017/S0266462303000163. PMID 12701949.

   Thank you for your suggestion. Savoie et al recommended that electronic search of trial registry, hand-search of reference list, specialist database search and internet search will be able to identify additional RCTs of lipid-lowering trials and acupuncture project trials.

   In compliance with our original protocol, we did not only search several general databases, we also searched clinical trial registries and hand-searched the reference list as suggested by Savoie et al (see page 6 line 9-17). Indeed, we reported the additional trials were identified from clinical trial registries (see page 16 line 14-16).

   We identified different types of journal articles including editorials and conference abstracts. However, our protocol excluded conference abstracts as we were unable to assess the quality of these studies. Nevertheless we accept the reviewer’s next comment and included some results of conference abstracts for discussion.

3. 11 abstracts have been presented to the EULAR congress, you much better study them and consider them in the case of relevancy for measuring the publication bias to improve the power of your results (as they are including negative results regarding the safety of tofacitinib).
Thank you for your comments. We agree with the reviewer that the conference abstract may present some negative results regarding the safety of tofacitinib, therefore we discuss two of them with relevancy in our discussion part. Please refer to page 15 line 1-3 and 8-12.

However, the conference abstracts may vary in methodological rigor and quality as they have not yet been adequately peer reviewed. It would not be appropriate to combine data with other published high quality studies in our meta-analysis.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.
Reviewer's report

Title: Efficacy and safety of tofacitinib in the treatment of rheumatoid arthritis: a systematic review and meta-analysis

Version: 1 Date: 9 June 2013

Reviewer: RIEKE ALTEN

Reviewer's report:

I have no proposals for amendments
the article is well written and contributes to the understanding of the new drug tofacitinib

Review #2 has no suggested changes for the manuscript. Thank you.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I have received Research grants and honoraria from Pfizer
Reviewer's report

Title: Efficacy and safety of tofacitinib in the treatment of rheumatoid arthritis: a systematic review and meta-analysis

Version: 1 Date: 28 August 2013

Reviewer: Malinee Laopaiboon

Reviewer's report:

The paper is interesting and has a clear presentation in most parts of the paper. There is, however, inappropriate presentation in the analysis part. The authors present that 'Risk ratios (RR) and mean differences were calculated for dichotomous outcomes......' Mean differences are used for continuous outcomes, not for dichotomous outcomes.

Thank you very much for your comments. The sentence has been changed in the manuscript. Please refer to page 8 line 15.

Level of interest: An article of importance in its field

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.
Comments from the Associate Editor:

The paper is interesting and has a clear presentation in most parts of the paper. There is, however, inappropriate presentation in the analysis part. The authors present that 'Risk ratios (RR) and mean differences were calculated for dichotomous outcomes......' Mean differences are used for continuous outcomes, not for dichotomous outcomes.

Thank you very much for your comments. The sentence has been changed in the manuscript. Please refer to page 8 line 15.

Editorial Requirements:

We strongly urge you to make these changes promptly, as we cannot proceed to the next process until we have received a version containing the changes.

1.) Please clarify which tables you wish to be included in the manuscript and which should supplementary.

   We wish to include table 1, 2 and 3 in the manuscript while supplementary 1, 2, 3 and 4 are supplementary tables only.

2.) Kindly adhere to PRISMA guidelines, and please provide us with a completed copy of the PRISMA checklist for your study.

PRISMA ? Systematic Reviews http://www.prisma-statement.org/

   Enclosed please find the PRISMA checklist for our review study. Thank you.