Author’s response to reviews

Title: Malignancy risk in Australian rheumatoid arthritis patients treated with anti-tumour necrosis factor therapy: an update from the Australian Rheumatology Association Database (ARAD) prospective cohort study

Authors:
Margaret Staples (margaret.staples@monash.edu)
Lyn March (lyn.march@sydney.edu.au)
Catherine Hill (Catherine.Hill@sa.gov.au)
Marissa Lassere (m.lassere@unsw.edu.au)
Rachelle Buchbinder (rachelle.buchbinder@monash.edu)

Version: 1 Date: 08 Oct 2018

Author’s response to reviews:

Cong-Qiu Chu
BMC Rheumatology
http://bmcrheumatol.biomedcentral.com/

9 October 2018

Dear Dr Chu,

Thank you for your email regarding the status of our manuscript "Malignancy risk in Australian rheumatoid arthritis patients treated with anti-tumour necrosis factor therapy: an update from the Australian Rheumatology Association Database (ARAD) prospective cohort study" (BRHM-D-18-00046) and informing us that it is potentially acceptable for publication in BMC Rheumatology, once we have carried out some essential revisions suggested by your reviewers.
We conform that all author details on the revised version are correct, that all authors have agreed to authorship and order of authorship for this manuscript and that all authors have the appropriate permissions and rights to the reported data. Please note that as stated in our manuscript, the corresponding author is Prof Rachelle Buchbinder. Dr Margaret Staples has now retired. We are not sure how to alter this in the system.

Response to reviewers’ comments are below.

Reviewer reports:

Gregory Gardner (Reviewer 1): This is a well written and discussed manuscript reviewing the malignancy risk of patients with RA with our without exposure to TNF agents. Methods are clear and statistics appear appropriate for data analysis. The limitation of the paper are also, in general, well discussed. The concept and results are not unique and generally do not add anything new to our understanding of TNFi risk in the area of malignancy with the exception of the observed increased risk of lung cancer that has not generally been seen in multiple other studies. I would like to see a bit more discussion on lung cancer and RA and some speculation on the authors part to explain their data. The results though do add to the overall reassurance that TNFI are safe. The authors explain that participation in the database is voluntary. Is there any way to look at cancer risk among all RA patients in Australia given the required reporting to reassure the reader that this group is not somehow different that RA patients in general? If not easily done I would add this to the limitations discussion. Finally, the MOA of the fusion protein etanercept is a bit different than the monoclonal or monoclonal-like TNFis. Approximately 50% of patient on TNFis are on etanercept and the rest on the Mabs. They say there is not sufficient data to analyze individual TNFi but what about fusion protein vs Mabs?

We have added further discussion on lung cancer and RA as requested (line 196-199). Unfortunately there is no way of looking at cancer risk among all RA patents in Australia and we have added this to the limitations section (line 267-270). Similar to a lack of sufficient data to analyse individual TNFi, there are also insufficient data to analyse our data in the way that is suggested.

Jun-Feng Jia (Reviewer 2): In the present paper the authors assessed malignancy risk in a cohort of Australian RA patients relative to the Australian population and to compare cancer risk for patients exposed to TNFi therapy versus a biologic-naïve group. They were able to show that overall malignancy incidence was elevated for biologic-naïve RA patients but not for those exposed to TNFi. TNFi exposure did not increase malignancy risk beyond that experienced by biologic-naïve patients. Furthermore they demonstrated Lung cancer risk was increased for both TNFi-treated and biologic-naïve RA patients compared with the general population suggesting
that RA status or RA treatments other than TNFi may be responsible in some way. The manuscript is concise and presents interesting data.

We thank Reviewer 2 for their comments.

Your sincerely,

Rachelle Buchbinder
Corresponding author, on behalf of all authors