Reviewer's report

Title: Serum levels of reactive oxygen metabolites at 12 weeks during tocilizumab therapy are predictive of 52 weeks-disease activity score-remission in patients with rheumatoid arthritis

Version: 1 Date: 25 Jul 2019

Reviewer: Jennifer Humphreys

Reviewer's report:

1. The background requires greater explanation about why changes in CRP may not reflect true inflammatory burden. As far as I am aware, there is data suggesting IL-6 receptor blockade directly changes CRP, but you are hypothesising this may not be a true change in inflammation. The scientific rationale for this needs to be made more strongly in your introduction in order to justify the study. There should also be justification for why this would not happen with the reactive oxygen metabolites

2. Was there a washout period between patients stopping other biologics and starting IL-6?

2. Given that your data are mostly on-parametric and you are using Mann Whitney, it would be more appropriate to report median and inter-quartile ranges. At the moment it looks odd that a tender joint count is reported as 4.7 +/- 6.6, as that implies that you could possibly have a TJC of -1.9

3. In tables, you should include what parameters are being reported (e.g. in tables 2 and 3, I think these are means and standard deviation but I don't know)

4. Please report what variables were adjusted for in the logistic regression. This should be included in the methods and be documented in table 4. It is important to know what variables were considered for selection by the stepwise model. The numbers in this study are very small, and there is a risk of finding a statistically significant result due to multiple testing rather than a true association

5. I think the opening line of your discussion is on overstatement of the results. The numbers are small and you only found an association with one of your outcomes. The data clearly need replicating on a larger scale before definitely being described as "useful".

6. In your discussion you mention that IL-6 levels are a better marker of inflammation in patients on tocilizumab. If that is the case and has been demonstrated, why should the ROM test be developed or measured, why not just use IL6 levels? No justification for this is provided in the discussion.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

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