Reviewer’s report

Title: Adverse Infusion Reactions to Rituximab in Systemic Lupus Erythematosus: A Retrospective analysis

Version: 0 Date: 27 Nov 2018

Reviewer: Laura Ross

Reviewer's report:

This study addresses a question of clinical importance to clinicians treating patients with SLE.

The manuscript would be improved if the statistical significance of the differences between the patient characteristics in the no reaction vs IR groups were presented. It is difficult to draw conclusions about the differences in these patient populations with only numerical differences are presented. There is one p value presented in the discussion section, this should be in the Results section and the p-values for the differences should be presented as an extra column in table 1. The statistical test used to compare each group should be stated in the Methods section. Also, it is unclear what 1 2 3 4 ENA refers to in Table 1.

It would be useful to know what other concurrent medications patients were receiving and whether this had any effect on IR. This is particularly relevant for cyclophosphamide which was given as per institutional protocol for some of the time reviewed in this study. Was there a difference in the number of IR in patients receiving cyclophosphamide? Did this increase or decrease the rates of RTX IR? Reference is made within the text to some reactions being excluded from analysis because of concurrent administration of cyclophosphamide. How many infusions included in the analyses were co-administered with cyclophosphamide and RTX? How was it determined which infusions co-administered with cyclophosphamide were to be excluded? Given this is a retrospective analysis of IR, including delayed reactions, attribution of IR is difficult, particularly when a drug is co-administered with cyclophosphamide given its high toxicity. Also, the one death in your study is variably referred to as a complication of cyclophosphamide therapy and a RTX IR. If this was thought due to cyclophosphamide, why was this included in table 3 listing the severity of RTX IR?

Can a comment be made about the treatment response to these patients given RTX? Reference is made to 50% of patients with IR being not treated with further RTX for an unknown reason, could this be because they responded to RTX and didn't require any further therapy? A response rate of 50% would be consistent with the response rate for treatment with RTX from your centre quoted elsewhere in the paper. It is worth commenting on the observation that whilst a high number of patients who had a RTX IR were not re-treated, numerically, the patients who experienced an IR received the same number of cycles of RTX as those who had no reaction, from Table 1.

What was the compliance with pre-medications? Did this have an effect on IR rates? Is it possible to obtain this information from the electronic medical records reviewed for this study? Patients were
most likely to have an IR with their 2nd infusion, could this be in part attributable to the faster infusion rates used for the second RTX infusion?

It would be useful to quote the infusion reaction rates for other rheumatological conditions such as RA and ANCA vasculitis. How significant is the difference between the IR noted in this study compared to the published data in other rheumatological conditions?

Can a comment be made about why the IR rate was so much higher in this study compared to the cohort study from your centre quoted in your paper (17.6% vs 6.1%)?

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

No

**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 recommend additional statistical review

**Quality of written English**
Please indicate the quality of language in the manuscript:

Acceptable

**Declaration of competing interests**
Please complete a declaration of competing interests, considering the following questions:

1. Have you in the past five years received reimbursements, fees, funding, or salary from an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?
2. Do you hold any stocks or shares in an organisation that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

3. Do you hold or are you currently applying for any patents relating to the content of the manuscript?

4. Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

5. Do you have any other financial competing interests?

6. Do you have any non-financial competing interests in relation to this paper?

If you can answer no to all of the above, write 'I declare that I have no competing interests' below. If your reply is yes to any, please give details below.

I declare that I have no competing interests.

I agree to the open peer review policy of the journal. I understand that my name will be included on my report to the authors and, if the manuscript is accepted for publication, my named report including any attachments I upload will be posted on the website along with the authors' responses. I agree for my report to be made available under an Open Access Creative Commons CC-BY license (http://creativecommons.org/licenses/by/4.0/). I understand that any comments which I do not wish to be included in my named report can be included as confidential comments to the editors, which will not be published.

I agree to the open peer review policy of the journal