Reviewer’s report

Title: Immunoglobulin abnormalities are frequent in patients with lupus nephritis

Version: 0 Date: 01 May 2019

Reviewer: Ioannis Parodis

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In this research article, Maria-Jose Cuadrado and co-workers calculated the rates of aberrant immunoglobulin levels in patients with lupus nephritis. I have the following concerns and suggestions.

1. In the Background, the authors make a number of statements without providing references to support them, e.g. that hypogammaglobulinaemia is gaining recognition as a complication following B cell depleting therapy, or that patients with lupus nephritis are likely to "have multiple factors contributing to immunoglobulin abnormalities". Could the authors explain which these factors are and provide the appropriate references?

2. What was the aim of the study? There is no clear junction between the Background and the Methods. What is the knowledge gap and what is the question?

3. Please provide a Table with the patient characteristics, including disease duration and activity at the time of nephritis and Ig level testing. Were these cases incident or recurrent nephritides? It is not clear when the Ig testing was performed in relation to the renal biopsy.

4. It would be informative to provide the readers with the treatment regimens used as induction and maintenance therapies for the patients' nephritides, as well as the ISN/RPS lupus nephritis class and NIH activity and chronicity index scores. E.g. cyclophosphamide is not mentioned in the list of regimens in the Methods, but is discussed in the Results (last sentence). It is not clear to this reviewer when and why cyclophosphamide was used to that specific patient.

5. What treatment(s) were patients who showed aberrant immunoglobulin levels receiving and for how long? What was the current dose and cumulative exposure to glucocorticoids?

6. Could the authors also provide leukocyte counts (total and different lines), especially in the patients with aberrant Ig levels?

7. How many patients of the ones surveyed here received rituximab at a later stage?

8. IgG has a molecular mass that is double as high as the one of albumin. How possible (or impossible) is it according to the authors that the association between
hypogammaglobulinaemia and nephrotic syndrome is due to IgG losses? In either case, how does Ig monitoring guide the choice of treatment?

9. Again, if post-rituximab hypogammaglobulinaemia is not associated with increased frequencies of infections, why is it important to monitor IgG levels?

10. It is unclear to this reviewer how the authors end up with the recommendation that clinical immunologists (rather than rheumatologists) should assess the suitability for Ig therapy.

11. The authors may want to consider revising their article to a Review article summarising current literature on Ig aberrancies.

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.

Yes

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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