Reviewer's report

Title: Intravenous Pulse Methylprednisolone For Induction Of Remission In Severe ANCA Associated Vasculitis: A Multi-Center Retrospective Cohort Study

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Reviewer: Jan Stephan Sanders

Reviewer's report:

Chanouzas et al describe outcome of a retrospective cohort of 114 patients with severe AAV who were treated with cyclophosphamide, prednisolone, plasmapheresis. In 52 of these patients methylprednisolone was added.

The authors did not find a clear benefit of MP treatment, but MP treatment was associated with an increased risk of infection and a higher incidence of diabetes.

This study fills a gap in the existing literature as no evidence is currently available on the merit of MP in the treatment of patients with severe AAV.

I have several comments:

1. 5 centers included patients, how was treatment with additional methylprednisolone divided over these centers? Was there a center difference in indication for or dosage of methylprednisolone therapy?

2. In the baseline characteristics BVAS at baseline is not included, please include this; and consider including this in the analysis regarding propensity scores.

3. There was a striking difference in the total cyclophosphamide dose between the patients with and without methylpred treatment, please elaborate on this. Was there also a difference in number of patients that received iv or oral cyclophosphamide between MP and non-MP treated patients.

Could patients who received methylpred have reached remission earlier than patients who did not receive MP? Time to remission could be added as additional secondary end-point.

4. Additionally, there was a significant difference in cumulative steroid dosage between the two groups, even to such extent that adding the methylprednisolone dosages to the oral prednisolone dosages results in similar steroid dosages at 12 months. As the end-point was set at 3 months it is important to know what the steroid dosage at 3 months was. And again, could patients who did receive MP have reached remission earlier than patients who did not receive MP?
5. As the oral dose of prednisolone was also associated with the risk of infection at 3 months, could methylprednisolone and prednisolone be interchangeable in their effect on this risk? Are MP and prednisolone treatment true independent variables, or are these redundant in this analysis? Please clarify or adapt this analysis.

6. Page 10: "…commencement of therapy as can be seen in Figure 2": should refer to figure 3

**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.

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 recommend additional statistical review

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