Reviewer’s report

Title: Quantification of Cancer Risk in Glomerulonephritis

Version: 0 Date: 28 Aug 2017

Reviewer: Navin Jaipaul

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This is a descriptive study of prevalent and incident cancer diagnoses observed in patients with biopsy-proven glomerulonephritis (GN) over a 20-year period, before and after the midpoint of GN diagnosis, extracted from two Danish renal biopsy registries and linked to cancer diagnoses in the Danish Cancer Registry. The authors report increase in cancer rates observed for most varieties of GN, particularly membranoproliferative GN in the older cohort over age 64. Due to their findings, the authors conclude that Nephrologists should consider expanding cancer screening for GN beyond the current standard practice for membranous nephropathy.

Several concerns necessitating major revisions:

1. While the study benefits from a large population in a well-established and validated cohort of patients, the cancer risk stratified by GN category is expressed by observed and expected rates rather than risk ratios which would be more clinically relevant measures.

2. Of particular concern relating to study validity are conflicting results which are inconsistent with other reported and well accepted associations of GN and cancer in the literature. The authors also point this out, but their explanations are not sufficiently convincing to reconcile the discrepancy.

3. The study appears to lack adjustment for other factors which may contribute to the incident development of cancer in GN patients, such as treatment with immunosuppressive medications, comorbid conditions like HIV and Hepatitis C which lower immune tolerance, and advancing age. This residual confounding prevents evaluation for an independent association of GN with incident cancer diagnosis.

4. Relevant baseline demographics of the study population have not been presented.

5. Due to these limitations, the study is not designed to determine incident cancer risk or screening indications for patients with GN and the conclusions are not supported by the data.

6. Results may not be generalizable to other populations.

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 am able to assess the statistics

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

Needs some language corrections before being published

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