Reviewer's report

Title: Effect of CYP3 A4, CYP3 A5 and ABCB1 gene polymorphisms on the clinical efficacy of tacrolimus in the treatment of nephrotic syndrome

Version: 0 Date: 02 Nov 2017

Reviewer: Chun Shing Kwok

Reviewer's report:

Dear Editors and Authors,

Thank you for this opportunity to review this manuscript on the effect of gene polymorphisms on the efficacy of tacrolimus in patients with nephrotic syndrome.

I am not an expert of genetics or renal medicine but I can provide a general review of the article from the perspective of a general physician. I think the paper should be reviewed by at least one renal physician.

My comments are as follows:

1) The title should include something about tacrolimus treatment

2) The abstract methods should include more in the methods to describe clearly the population (patients with nephrotic syndrome treated with tacrolimus, the exposure (genotype differences) and outcomes (response to treatment). The method of analysis (multivariable logistic regression) should be described.

3) The abstract results should state the number of patients and number of patients with each allele type (not just percentages).

4) The abstract results should also state not just odds ratios and p-values but 95% confidence intervals.

5) The abstract results contain repetition as both the odds ratio/p-values and text description. I would keep the text description and put the odds ratios, 95% confidence intervals and p-values in parentheses after each numerical result.
6) Tacrolimus is not a novel agent as it has been around for a long time but its application in nephrotic syndrome.

7) A key issue with the study is that nephrotic syndrome is relatively non-specific term. The cause of nephrotic syndrome is important whether it was mainly minimal change disease, focal segmental glomerulosclerosis, membranous, etc. This should be specified in the study.

8) First paragraph of Background can be shortened. It should explain why nephrotic syndrome is important. It should explain that tacrolimus can be used to treat it. It should explain the relevance of genetic polymorphisms on efficacy (Is this the first study to look at this?). The second paragraph should explain what is known in the current literature about gene polymorphisms and response to tacrolimus treatment in nephrotic syndrome and it currently talks about transplant patients.

9) Please explain how nephrotic syndrome aetiology was determined. Was renal biopsy performed?

10) Please explain how the sample size was determined. A power calculation should be performed. Considering the large confidence intervals the study looks underpowered.

11) Please state in the methods the approvals that were sought for the conduct of the study and the ethical approval. Also state how informed consent was obtained.

12) Please explain how the statistical analysis as performed and what factors were adjusted for in the logistic regression.

13) What is the definition of effective treatment? This should be stated in the methods. The evaluation of safety should also be stated in the methods.

14) The results should not contain explanation of what was done. That should be in the methods.

15) The discussion first paragraph should state what the main findings of the study are and the clinical implications. The second paragraph should state how it compares to existing literature. The next paragraph should talk about the mechanisms of the findings. Other interesting findings can be described in other paragraphs like mutation frequency differing from general population, how does cause of nephrotic syndrome influence clinical efficacy and clinical efficacy of tacrolimus in other settings. There should also be a paragraph about strengths and limitations about the study. The study should finally have a conclusion paragraph.
16) I think a native English speaker should go through the text. Words like for researches are generally not used.

**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.
Unable to assess

**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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