Reviewer's report

Title: Chronic Asymptomatic Pyuria Precedes Overt Urinary Tract Infection and Deterioration of Renal Function in Autosomal Dominant Polycystic Kidney Disease

Version: 2 Date: 12 November 2012

Reviewer: Andreas Kistler

Reviewer's report:

The authors have addressed most of my criticisms and added additional analyses. My major criticism remains that I believe asymptomatic pyuria might be more a marker of progressive disease than a cause for accelerated GFR decline and I think that this issue merits a more critical discussion.

Major Compulsory Revisions:

The authors now provide an additional analysis defining the pyuria and non-pyuria groups based on the first year of follow up, as I had suggested. These groups did not differ with respect to GFR decline during further follow up. In their response to my comment, the authors suggest that one year may not be enough to show the impact of recurrent pyuria on renal function. However, these patients were followed for much more than a year after the first year of follow up on which the group definitions were based. I rather think that this new additional analysis suggests, as I had suspected, that pyuria is likely not the cause of future GFR decline. I still believe that the greater GFR decline in Group B is just due to the fact that group B comprised patients that were followed until they had more advanced disease and that these patients were more likely to experience asymptomatic pyuria due to more advanced disease and pyuria was more likely to be detected due to more frequent controls.

Therefore, I think the authors should take more emphasis away from the point that pyuria may contribute to GFR decline in ADPKD. Also, they should state the rationale for performing the new analysis based on the first year of follow up and discuss the probable possibility that more frequent diagnosis of pyuria was a consequence rather than a cause of progressive disease. Another additional analysis of interest, which could clarify this point, would be to check whether asymptomatic pyuria became more common over time (with disease progression) within individual patients.

Although the hypothesis of pyuria leading to GFR decline in ADPKD patients is interesting and might be true, I do not think that the design of the current study does really support this hypothesis (due to the reasons outlined above).

Minor Essential Revisions:

The authors gave the frequency of patient visits in their response letter, but I
think this information should also be included in the methods section.

Discretionary Revisions:

Page 9, 2nd para: I would add the percentage of negative cultures (can be calculated from the numbers given, but makes it easier for the reader if this number is given directly).

Page 9, bottom: “In addition, when we used the new prospective groups” leave away “new” since the reader of the article will not know that this analysis has been added for the revision of the article and the groups are therefore “new”. Same for page 11, top.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests