Reviewer's report

**Title:** Effect of paricalcitol on renin and albuminuria in non-diabetic stage III-IV chronic kidney disease: a randomized placebo-controlled trial

**Version:** 2  **Date:** 9 April 2013

**Reviewer:** Ishir Bhan

**Reviewer's report:**

The authors describe a randomized control trial of paricalcitol on the renin-angiotensin-aldosterone axis and albuminuria in non-diabetic pre-dialysis CKD.

In this small study (n=26), the authors find that albumin excretion was reduced and the L-NMMA-associated albuminemic response was tempered by paricalcitol. However, no change in the RAA axis was observed.

The study appears well designed. It is a randomized trial with appropriate block randomization, includes a run-in period to clear vitamin D and RAS inhibitors. Blood pressure medications are held stable. A standardized diet is used and intake is tightly regulated.

**Major Compulsory Revisions**

In the abstract, the statement "FGF23 increased by 46%" should be rephrased to compare the change FGF-23 in placebo vs paricalcitol arms. It's not clear from the abstract if 46% refers to the difference between the arms or the change from baseline in the paricalcitol group. In general, the within-group comparisons should also be done between groups, since this is a randomized trial.

In the results, the authors state "Absolute 24-h urinary albumin excretion did not decrease significantly after paricalcitol (-7% [95%CI:-20;7], Table 4). During the baseline periods of the clearance experiment, albumin excretion rate was reduced significantly by 19% [95%CI:-31;-8] (p=0.003) and UACR by 20% [95%CI:-30;-11] (p<0.001) compared with placebo."

This is an important result, but one of the most confusing sections of the paper. It may help to specifically highlight the differences both in time and methodology of these two results. A reference to Table 1 may help here, but more description may also help. For example, the authors reference the "clearance experiment", but it's not explicitly labeled as such in Table 1, so readers may be left confused.

It will also be helpful in the discussion section to review this discrepancy in findings.

**Minor Essential Revisions**
"Selective VDRAs such as paricalcitol effectively suppresses", the last word should be "suppress" since the subject is "selective VDRAs such as paricalcitol"

Discretionary Revisions

While interesting, it is not clear why FGF-23 is included in this analysis or how it relates to the primary focus of the study. Perhaps the authors could clarify or remove FGF-23 from the abstract.

The introduction might explain why the study was done only in non-diabetic patients.

Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests