Reviewer's report

Title: High Serum Bicarbonate Level within the Normal Range Prevents the Progression of Chronic Kidney Disease in Elderly Chronic Kidney Disease Patients

Version: 2 Date: 9 November 2012

Reviewer: Julia Scialla

Reviewer's report:

The authors have responded to many of the issues raised in the initial review, but I still have a few comments.

Major Compulsory Revisions

1. Since this study occurred in a real life clinical setting and not in the setting of a study protocol, the number of eGFR measurements for each participant likely varied based on how closely a patient needed monitoring. This may dramatically affect when patients achieve the endpoint of a 25% reduction in eGFR. Can you please provide information on the distribution of eGFR frequency and how this differed in the two groups? I am concerned that the low bicarbonate group had more advanced CKD, more refractory acidosis and may have had much more frequent measurement of eGFR.

2. How many events were eGFR versus ESRD events by group?

3. I am not convinced of the usefulness of the univariate logistic model. What is the contribution of this result? There are large differences in eGFR across bicarbonate levels so without adjustment for GFR, no real inference can be made about the importance of the bicarbonate here.

4. The discussion needs to address the fact that this population includes both treated and untreated subjects. In fact the proportion treated and dose of bicarbonate used is much higher in the low serum bicarbonate group. It could be that aggressive sodium loading with sodium bicarbonate is harmful in this study or that "refractory" acidosis is harmful whereas easily treated is not. Ideally the treated and untreated populations would be evaluated separately but the sample size is probably not large enough to do this.

Minor Essential Revisions:

1. The description of the study protocol remains somewhat confusing. This was a retrospective study and therefore I would not expect that patients were treated according to any pre-specified study protocol. This is somewhat misleading in the study design and study population section of the manuscript. In particular the following statement may require clarification: "We treated CKD in accordance with the CKD practice guideline of the Japanese Society of Nephrology. A high serum bicarbonate level was treated in accordance with K/DOQI guidelines 2000."
By administration of only sodium bicarbonate, serum bicarbonate level was maintained from 22-32 mEq/L. It might be more appropriate to state that this was the general practice of the clinic to follow such clinical practice guidelines, but I suspect this was not protocolized for this study.

2. Several places in the manuscript use the language that "an increase in serum bicarbonate level decreased the risk of CKD progression." This suggests cause and effect and should be revised to state that "a higher serum bicarbonate level was associated with lower risk of CKD progression." This language is used throughout the manuscript: abstract, results and discussion.

**Level of interest:** An article of limited interest

**Quality of written English:** Not suitable for publication unless extensively edited

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

**Declaration of competing interests:**

Nothing to disclose.