Reviewer's report

Title: The value of maintaining normokalaemia and enabling RAASi therapy in chronic kidney disease

Version: 0 Date: 09 Dec 2018

Reviewer: Navin Jaipaul

Reviewer's report:

The authors developed a patient-level simulation model to characterize the lifetime natural history of CKD and predict outcomes as a function of serum potassium level and RAASi use. They demonstrated that maintenance of normokalemia to allow optimization of RAASi therapy was associated with delayed CKD progression and RRT initiation, improved quality of life and survival, and cost savings.

The manuscript is well written and study design robust. A useful clinical model should demonstrate predictive ability and validity in evaluating meaningful outcomes where assumptions are reflective of actual practice. The base case analysis assumed optimal dosing of RAASi to achieve the full benefit of therapy observed in clinical trials, with scaled efficacy assessment to account for a range of suboptimal dosing that may be common in clinical practice. The findings support the notion that normokalemia with RAASi optimization results in improved outcomes, but the intervention to achievement of normokalemia is open-ended and leaves many unanswered questions. Consequently, the clinical utility and relevance of such a model may be limited and largely hypothetical. Implications of the findings should be interpreted with caution. For example, certain practices may fall outside the standard of care (like combination therapy with ACEi and ARB) that may be interpreted to be permissible if normokalemia is achieved. Authors should further elaborate on these limitations and the generalizability of results.

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