Reviewer's report

Title: Treatment with Nesiritide is Not Associated with Positive Outcomes in Patients Hospitalized for Acute Decompensated Heart Failure

Version: 1 Date: 20 July 2007

Reviewer: jonathan Sackner-bernstein

Reviewer's report:

General

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Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)

The authors should provide more information to explain why the outcomes appear worse for mortality when using the MEDai models as opposed to the APR-DRG models. This inconsistency in the mortality effect should be discussed as making this finding less robust, and the two approaches should be compared to the ADHERE registry analytic approaches.

MEDai: The authors cite the use of the method in a pneumonia analysis and report on page 8 that the technique was validated. Perhaps this validation methodology and results could be made available as an online supplement. Did it include unique groups of patients for the derivation and validation? Were any of the patients that are part of the analysis set of this paper also part of those derivation and validation sets? Why do the authors want readers to put more weight on the MEDai than the APR-DRG model?

The results section portrays the use of nesiritide as one with increased risk of mortality, prolonged length of stay, increased costs and point estimates suggesting even the possibility of increased readmission rates. Yet the authors have not divulged how many events there actually were. By my calculation, there were only 13 deaths in the nesiritide treated population. Such a small number means that errors are possible which may be reflected in the results being somewhat different using the two methodologies for mortality risk estimates. Can the authors provide the number of events?

The authors state an interpretation of the study findings in the title. There are reasons to advocate for a different tact. First, the tone is one where it seems that the paper will “prove” this to be the case, when some could argue that this analytic approach cannot be claimed as proof. Second, the analyses are also relevant for showing that nesiritide is not so clearly associated with risk. This manuscript provides justification for continuing enrollment in the ongoing clinical outcomes trial assessing nesiritide, as one can point to these data as supporting that the trial is ethical.
Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)

On page 11, the authors focus on the decreased use of nesiritide in clinical practice. Citing the paper by Hauptman et al from JAMA would seem ideal.

When the authors refer to the meta-analysis from Sackner-Bernstein et al, it would be best to also cite the follow-up analysis also published in JAMA that includes more data and provides a more accurate estimate of risk.

Discretionary Revisions (which the author can choose to ignore)

On page 14, the authors state that nesiritide improves dyspnea. In fact, review of the data from VMAC will show that this is somewhat of a marginal effect from both a statistical and especially clinical perspective. One could argue whether this should be stated with the same conviction as the hemodynamic effect, merely because the approved labeling says them in this fashion.

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

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:

My dependent children hold nominal shares of Johnson & Johnson stock in custodial accounts. I acknowledge past efforts calling for withdrawal of nesiritide from the market. I do not believe that I have biases affecting my review of this article, and receive no funding from Scios or J&J.