Reviewer's report

Title: Prognostic impact of three immunohistochemically detected markers of neuroendocrine differentiation in prostate cancer

Version: 3 Date: 4 December 2008

Reviewer: Andrew Roddam

Reviewer's report:

This paper presents data from a study of NE differentiation in prostate cancer as a potential prognostic marker. The data consist of a series of 95 specimens from 84 patients. I have a number of concerns about this paper.

1. The sample size for a prognostic marker study is very small. This presents the authors with a number of critical problems. Firstly the small sample size does not permit the authors to investigate whether or not the markers they have investigated are related to prognosis after adjustment for other known prognostic variables, by use of for example a cox regression model. Secondly if they had been able to come up with a predictive/prognostic rule it is normal to develop this on a training set of the data and then validate its use on a validation set – again this is not possible with the current data.

2. The authors have used 95 samples from 84 people but it does not appear that they have accounted for the correlations that will exist due to multiple samples from the same person.

3. The presentation of the results in Table 1 make it very difficult to interpret. It is not clear which of the results are significant, what the p-values are.

4. The selective presentation of the results for CgA in Table 2 also make it difficult to interpret the overall outcome of the study. Why not also show the results for the 2 other NE markers. Further as stated in point 1 above, it is essential to see if there are differences after adjustment for other prognostic factors.

Overall I feel that the paper, with the data set available to the authors, can do little more than report on the correlations between some NE markers and other clinical characteristics of patients. It is not able to assess the prognostic validity.

Level of interest: An article of insufficient interest to warrant publication in a scientific/medical journal

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