Reviewer's report

Title: A panel of kallikrein markers can predict outcome of prostate biopsy following clinical work-up: an independent validation study from the European Randomized Study of Prostate Cancer screening, France

Version: 2 Date: 4 August 2010

Reviewer: Robert Den

Reviewer's report:

The study conducted by Benchikh et al. was a validation study of their panel of four kallikrein markers which they had previously demonstrated to be highly predictive of prostate cancer in men for whom the decision to biopsy is based on clinical work-up. Their model had a higher rate of predictive accuracy than the base model (area-under-the-curve improved from 0.63 to 0.78) for all prostate cancer and for high gleason prostate disease (Gleason >7).

I thought that the study was straightforward and well done. It is refreshing to see a validation study of biomarkers. However, in reviewing the literature, it appears that this model has been validated in other datasets already. This study did not advance this idea further.

1. The authors thoughtfully examine the details of further diagnostic workup of men with an elevated PSA in Table 1. I would like to see some analysis of either cost-function or QALY for undergoing additional tests. This may speak to the additional benefit that a more predictive assay would bring.

2. Further, in the original ERSPC trial, overall survival and prostate cancer specific survival was reported. I would like to see how the kallikrein markers would impact on survival. Although, gleason score is a surrogate for aggressive disease, there is not a direct relationship to death from prostate cancer.

3. I would like to see the authors give more insight into how the base model and kallikrein model predict the AUC that they report. I understand that it is reported in a separate manuscript, but it would be beneficial to restate it in a few sentences within this manuscript.

4. I think that it would be beneficial to comment on how this might be used prospectively in a trial to truly validate the benefit in terms of prostate cancer mortality.

Level of interest: An article whose findings are important to those with closely related research interests

Quality of written English: Acceptable
**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests.