Reviewer's report

Title: Prognostic implications in the shift of Syndecan-1 expression from the cell membrane to the cytoplasm in bladder cancer

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Reviewer: Lars Dyrskjot

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Makito et al describe SDC-1 expression in urine from patients with bladder cancer (n=102) and from healthy individuals (n=206). The authors found no diagnostic value of SDC-1, but found that significant differences were present between patients with tumors of different stages and grades. Using IHC it was shown that the difference between stage and grade was associated with a shift from the cellular membrane to the cytoplasm. Univariate analyses showed that SDC-1 was significantly associated with disease-specific survival, however, multivariate analysis showed that only muscle invasive bladder cancer was a significant predictor of survival.

Overall, as the findings of a shift in cellular localization of SDC-1 is mainly associated with known risk parameters like stage and grade, and multivariate analysis does not show any independent prognostic value, the description of prognostic value of SDC-1 should be changed (e.g. the title of the paper).

Major Compulsory Revisions:
1. How is the 8 benign tissue characterized, which patients do the tissue originate from and how were they diagnosed?
2. As most of the results in this manuscript is based on the antibody against SDC-1, the authors should verify the specificity by Western blotting.
3. Two investigators reviewed IHC scorings – the Kappa score for inter observer agreement should be calculated and presented.
4. The authors should present the details of the multivariate analysis. Which parameters were included etc. The 95% CI presented describes a huge range of the HR – were assumptions of proportional hazards verified before analysis?

Minor Essential Revisions:
1. Some language correction is needed on page 5: “Paraffin blocks...” and the following two sentences.

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

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'