Reviewer's report

Title: Reduced expression of ezrin in urothelial bladder cancer signifies clinically advanced disease, tumour progression and an impaired survival: validatory study of two independent patient cohorts

Version: 1 Date: 24 March 2014

Reviewer: Jose Mansure

Reviewer's report:

Major compulsory revisions:

1. The questions posed by the authors are well defined, but the authors have not provided sufficient analytical evidence of subject importance.

2. The analysis does not record competing events (e.g. death from other causes) prior to disease specific death. A competing risk regression should be considered.

3. In table 1, the number of patients and their respective percentages should be presented for each clinicopathological factor. This will help the readers to evaluate factor distribution in each cohort.

4. All of the K-M figures must include a "risk-table" showing the number of patients at risk during each time span.

5. The methodology of Classification and Regression Tree (CRT) analysis, which has been used to assess the optimal prognostic cut-offs for ezrin expression, should have a more elaborate description.

6. Furthermore, interpretations (discussion and conclusion) made by the authors seem unbalanced and inadequately supported by the data. For instance, the authors conclude that reduced membranous ezrin is associated with reduced survival. However, when the multivariate analysis was performed, this association was only marginally retained as an independent prognostic value for 5 year OS in the smaller cohort. It seems unlikely that the lack of an independent prognostic value of ezrin expression in the larger cohort is due to its strong link to tumor grade and stage as the distribution of tumor stage and grade in both cohorts are not significantly different [Reference 22-23] to fully support the hypothesis stated by the authors in the second paragraph of the discussion.

Level of interest: An article of limited interest

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