Reviewer’s report

Title: An evaluation of the real world use and clinical utility of the Cxbladder Monitor assay in the follow-up of patients previously treated for bladder cancer

Version: 0 Date: 18 Nov 2019

Reviewer: Jeremy Y. C. Teoh

Reviewer's report:

Thank you for your submission. This is a study investigating the performance of CxBladder monitor assay for bladder cancer detection upon surveillance.

I have the following questions / comments
1. There should be more descriptions on CxBladder monitor assay. What is it? How much urine is needed?
2. What is the usual flexible cystoscopy surveillance protocol in patients with high-risk disease?
3. For those with low-risk disease, but CxbM positive, will they follow the surveillance protocol as in the case of high-risk disease?
4. If CxbM is positive but cystoscopy is negative, will random bladder biopsy or repeat upper tract imaging be performed?
5. If CxbM is positive but cystoscopy is negative, will CxbM be done again upon follow up at all? I assume it will remain positive thereafter?
6. For low-risk disease, there may be missing data regarding the comparison of CxbM and cystoscopy results. Especially when you have alternative schedule, it seems impossible to have a fair analysis.
7. 257 low-risk patients provided 391 urine samples, but there were only 52 urine samples provided from 52 high-risk patients. It seems there is lack of longitudinal data especially for those high-risk patient. This must be clarified.
8. There is insufficient information regarding the disease characteristics. Number of tumours, size of tumours, grading, presence of CIS, any previous recurrence, etc.
9. There is insufficient information regarding the management of these patients. Any second look TURBT? Any BCG therapy? Etc.
10. The analyses performed were too simple. How about the sensitivity, specificity, NPV and PPV? How about the ROC curve, what is the AUC?
11. In the discussion part, there should extensive descriptions about the available urine biomarkers, and how does your marker compare with the existing markers.
12. You should probably discuss about the potential utility of urine markers, i.e. screening, primary diagnosis vs surveillance, and why you are focusing in surveillance only.

Please confirm that you have included your review in the ‘Comments to Author’ box?

As a minimum standard, please include a few sentences that outline what you think are the authors’ hypothesis/objectives, their main results, and the conclusions drawn. Your report should constructively instruct authors on how they can strengthen their paper to the point where it may be acceptable for publication, or provide detailed reasons as to why the manuscript does not fulfill our criteria for consideration. Please supply appropriate evidence using examples from the manuscript to substantiate your comments. Please break your comments into two bulleted or numbered sections: major and minor comments.
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Yes

**Are the methods appropriate and well described to allow independent reproduction of experiments?**
Please state in the ‘Comments to Authors’ box below what you think are the strengths and weaknesses of the methods (study design, data collection, and data analysis), and what is required, if anything, to improve the quality of reporting

Yes

**Does the work include the necessary controls?**
If not, please explain in the ‘Comments to Author’ box below.

No

**Are you able to assess the statistics?**
- Are the statistical test(s) used in this study appropriate and well described?
- Is the exact sample size (n) reported for each experimental group/condition (as a number, not a range)?
- Are the description of any error bars and probability values appropriate?
- Are all error bars defined in the corresponding figure legends?
- Has a sample size calculation been included, or a description and rationale about how sample sizes were chosen?

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No

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None

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