Reviewer’s report

Title: Recent Advances in the Treatment of Bladder Cancer

Version: 1 Date: 11 July 2012

Reviewer: Peter Black

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COMPULSORY

1. The abstract is a list of facts about bladder cancer – it needs some context. The title is the only hint of what the authors want to do here.

2. The Introduction is disjointed – it is a list of facts about bladder cancer that lead to the statement that the authors want to summarize recent advances. It needs to set the stage better for why this is a timely review and what the main issues in bladder cancer are. Also, why not include Cis with NMIBC? And what about BCG refractory T1 disease for cystectomy?

3. The discussion of each advance should include some sort of summary statement of where we stand now and what potential next steps might be. This “synthesis” is the key to a good review. For example, what do we do with the apparent contradiction with PDD that it detects more tumors but may not improve outcomes? The authors could mention here also the fact that these studies were done without post-TURB intravesical chemotherapy, which may further diminish the benefit of PDD. Also how do PDD and NBI compare? Some pros and cons of each would be helpful.

4. For the markers, there is little new about either NMP22 or Urovysion – except the article from Kamat on Urovysion for BCG response. Has anything in Table 1 changed over the past 5 years? Also, the authors cannot simply cite another review of markers as a sole reference for their own review. Again little synthesis here – how should we use these markers? Is there anything new out there? Why are we not more successful in adoption of markers?

5. The passage on dose reduction of BCG seems out of place. There are several “tricks” for reducing toxicity, including use of antibiotics and isoniazid, so why highlight dose reduction only? It is also a bit out of place coming right before a description of electromotive MMC, as if electromotive MMC was designed to improve BCG tolerability. Hyperthermia and EMDA are both promising – is it being adopted anywhere? Is it on trial only? Has it been approved for routine use anywhere? If not, why not, and what is the next step?

6. For intravesical gemcitabine, SWOG is just finishing a trial for single does post-op – so this should not be discounted. The authors should comment a little more about trials that have been done for adjuvant intravesical gemcitabine – here they give the context (promising but limited data), but not the data.
7. The RCT on robotic cystectomy by Nix has been criticised for very low numbers (inadequate power) – this should be mentioned in a review like this. Since one of the authors is a key member of the IRCC, the authors need to be careful about providing a balanced review of robotic cystectomy. “Motivated robotic surgeons” seems a bit embellished. On the other hand, this is a rapidly developing area of bladder cancer treatment and probably deserves more attention than the authors are giving it. Any idea, for example, on how widely RARC is being adopted in North America and Europe? The part about prospective trials that is currently in the Conclusions belongs in this section.

8. The section on bladder preservation reflects the usual urologist bias (as does the last sentence of the paper) – especially in the UK, from where the authors hail, radiation is not just for those declining or deemed unfit for surgery! The paper by James et al is significant and deserves more attention. Why should this not convince us in North America to do a lot more bladder preservation (as is already done in the UK)? If the authors consider chemorads inferior, they need to make that case, especially in light of the James paper.

9. The authors comment in the conclusion that mortality is declining from bladder cancer – this does not come out anywhere else in the text and is not referenced. This would be truly new! Otherwise the Conclusions reads a bit like a shopping list.

DISCRETIONARY

10. A couple of things come to mind that are not addressed:
   1. Work on identifying markers that predict response to neoadjuvant chemotherapy; eg. Dan Theodorescu’s Coxen model
   2. German and US trials on value of extended pelvic lymph node dissection
   3. Update on trials for adjuvant chemo – there have been several published recently (at least as abstracts)

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