Editorial

Urinary biomarker for the detection of recurrence following non-muscle invasive bladder cancer: are we there yet?

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A non-invasive urine based biomarker that is highly sensitive and specific is the ideal test to reduce the need for cystoscopy to detect bladder cancer. This is an area of much research with proof of concept reports showing a varying level of diagnostic accuracy using protein, genomic, transcriptomic and epigenetic based markers.

In this issue of the *British Journal of Urology International*, Pichler and colleagues reported the diagnostic accuracy of Xpert BC Monitor (Cepheid, Sunnyvale, CA, USA) as a cross sectional prospective observational study of 140 patients having cystoscopy as part of non-muscle invasive bladder cancer (NMIBC) surveillance (1). The Xpert BC Monitor represents a point of care polymerase chain reaction (PCR) based test interrogating 5 target mRNAs (ABL1, CRH, IGF2, UPK1B, ANXA10). In this study, the result of the Xpert BC Monitor was compared to urinary cytology which was evaluated using the Paris classification system, with cystoscopy representing the reference test. Pichler and colleagues report that Xpert BC Monitor had a superior overall sensitivity (84%), negative predictive value (NPV) (93%) and area under curve (0.87) compared to urinary cytology washings. In addition, sensitivity for low grade tumours was 77% although there was no difference in specificity (91%).

The Xpert BC Monitor platform is attractive for several reasons. It is a point of care test, requiring only 4 ml of urine and requires minimal hands on preparation time as it is automated. The single use disposable cartridges minimise cross contamination between different urine samples and are easy to use. With regards to its diagnostic accuracy, it successfully identified all but one high risk NMIBC (one pT1 tumour was missed) suggesting a high sensitivity. Identifying all high-risk bladder cancer is of paramount importance to allow early treatment and prevent disease progression. However, 7 of 31 low grade tumours were missed by the Xpert BC Monitor although a delay in diagnosis of these patients would pose a minimal risk (2). These results suggest a marginally better diagnostic accuracy compared to the six Food and Drug Administration (FDA) commercially approved urinary biomarkers with an overall sensitivity of 57–82% and specificity of 74–88% (3).

However, are such results sufficient to replace cystoscopy? The reason for the lack of uptake in urinary biomarker use is because none of the FDA approved tests are licensed for use as stand-alone tests without cystoscopy. The heterogeneous nature of bladder cancer suggests that a 5 panel biomarker may not be sufficient to identify all tumours (4). Other groups have reported biomarker panels ranging from 8 to 150 targets with a higher diagnostic accuracy (5,6). In addition, comparing the diagnostic ability of urinary cytology to Xpert BC Monitor serves little purpose. Urinary cytology only has value in high grade NMIBC as an adjunct to cystoscopy and not as a stand-alone test. The fact that nearly all high risk NMIBC

were identified suggest a role in the surveillance setting to increase the interval between surveillance cystoscopies as previously suggested (7,8).

Recommendations for NMIBC surveillance vary between guidelines and incorporating urinary biomarkers will require future studies to determine the best oncologically sound and cost-effective approach (9). While Pichler and colleagues should be congratulated for their study, many groups have reported different biomarker panels with impressive results. Hence, well-designed blinded prospective observational studies are required to validate such biomarkers before wide spread adoption (10).

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References

1. Pichler R, Fritz J, Tulchiner G, et al. Increased accuracy of a novel mRNA-based urine test for bladder cancer surveillance. BJU Int 2018;121:29-37.
2. Gofrit ON, Pode D, Lazar A, et al. Watchful waiting policy in recurrent Ta G1 bladder tumors. Eur Urol 2006;49:303-6.
3. Chou R, Gore JL, Buckley D, et al. Urinary Biomarkers for Diagnosis of Bladder Cancer: A Systematic Review and Meta-analysis. Ann Intern Med 2015;163:922-31.
4. Comprehensive molecular characterization of urothelial bladder carcinoma. Nature 2014;507:315-22.
5. Dahmcke CM, Steven KE, Larsen LK, et al. A Prospective Blinded Evaluation of Urine-DNA Testing for Detection of Urothelial Bladder Carcinoma in Patients with Gross Hematuria. Eur Urol 2016;70:916-9.
6. Feber A, Dhami P, Dong L, et al. UroMark-a urinary biomarker assay for the detection of bladder cancer. Clin Epigenetics 2017;9:8.
7. Chang SS, Boorjian SA, Chou R, et al. Diagnosis and Treatment of Non-Muscle Invasive Bladder Cancer: AUA/SUO Guideline. J Urol 2016;196:1021-9.
8. Ho CC, Tan WP, Pathmanathan R, et al. Fluorescence-in-situ-hybridization in the surveillance of urothelial cancers: can use of cystoscopy or ureteroscopy be deferred? Asian Pac J Cancer Prev 2013;14:4057-9.
9. Tan WS, Rodney S, Lamb B, et al. Management of non-muscle invasive bladder cancer: A comprehensive analysis of guidelines from the United States, Europe and Asia. Cancer Treat Rev 2016;47:22-31.
10. Tan WS, Feber A, Dong L, et al. DETECT I & DETECT II: a study protocol for a prospective multicentre observational study to validate the UroMark assay for the detection of bladder cancer from urinary cells. BMC Cancer 2017;17:767.

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