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## **Comparison of Different Analytical Platforms for the Identification of Tumor DNA in the Urine of Bladder Cancer Patients**

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### **Abstract: MP45-14**

#### **Introduction and Objectives**

Given the importance of surveillance in the management of non-muscle invasive bladder cancer (NMIBC), noninvasive detection of circulating or urine tumor DNA (utDNA) may improve and individualize the management of bladder cancer patients. Here we evaluate methylation-specific polymerase chain reaction (MS-PCR) and two next generation sequencing (NGS) approaches to identify the presence and association of utDNA with bladder cancer recurrence.

#### **Methods**

Urine was collected from 5 patients at the time of initial diagnosis of bladder cancer (positives), from 2 patients with prior NMIBC at the time of negative surveillance cystoscopy and from 1 patient pre-repeat transurethral resection with normal biopsy (total 3 negatives). DNA was isolated from fixed paraffin embedded primary tumors (FPET) from the eight patients - 4 high grade and 4 low grade – and from matched blood buffy coat cells, urine supernatant and urine sediment. Targeted NGS (covering <20,000bp) was performed on Ion Torrent (amplicon enrichment) and Illumina (hybridization capture) platforms, and MS-PCR performed with a panel of 13 assays. Percent utDNA was estimated from the ratio (urine:tumor) of single nucleotide variants (SNVs) or methylation sites compared to buffy coat.

#### **Results**

Tumor specific differentially methylated regions (DMRs) were found in 7 of the 8 FPETs compared to buffy coat. Tumor specific SNVs were found in 8/8 (Ion Torrent) and 6/8 (Illumina) FPETs compared to buffy coat. utDNA was found in 4 of the 5 positives by MS-PCR. There was complete concordance in all positive/negative calls for utDNA between the 2 NGS platforms, with utDNA found in 4 of the 5 positives and 0 of the 3 negatives. There was complete concordance in all positive/negative calls and estimates of tumor fraction between urine supernatant and urine sediment (within patient/technology).

#### **Conclusions**

Tumor specific DMRs and/or somatic SNVs were detected in 100% of NMIBC tumors using a MS-PCR gene panel and targeted NGS. Most events in utDNA were also observed in NMIBC tumor tissue at the time of diagnosis. These results provide early evidence that genetic and epigenetic events are evident in utDNA and reflect the presence and genetics of the NMIBC.

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