Abstract #: 846

Blood- and Urine-Based ctDNA Profiling and Monitoring in Bladder Carcinoma In Situ

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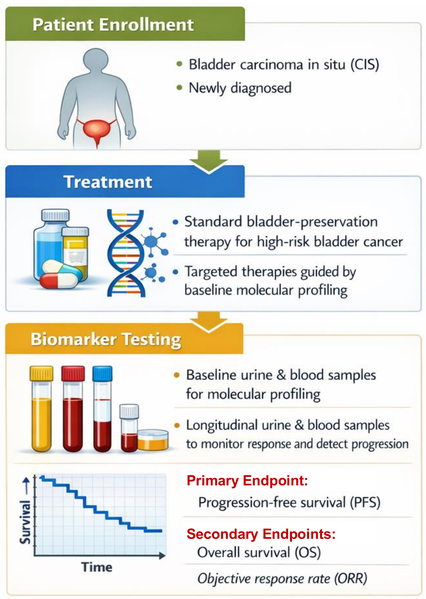
INTRODUCTION

Carcinoma in situ (CIS) of the bladder is an aggressive, high-grade, flat urothelial carcinoma associated with a substantial risk of recurrence and progression. Its management typically requires intensive surveillance and treatment, including frequent cystoscopic evaluations, which are both invasive and costly. Liquid biopsy has emerged as a promising non-invasive approach for the detection and monitoring of bladder cancer. In particular, analysis of circulating tumor DNA (ctDNA) enables the identification of tumor-specific genetic alterations shed into bodily fluids. As bladder tumors release ctDNA into both the bloodstream and urine, these biofluids represent accessible sources for molecular profiling. This study employs a next-generation sequencing (NGS)-based ctDNA assay to characterize somatic mutations and copy number alterations in patients with bladder CIS, utilizing both blood and urine samples for longitudinal monitoring.

METHODS

In this ongoing prospective study, patients with CIS bladder cancer were enrolled, and paired blood and urine samples were collected prior to initiation of first-line treatment. Additionally, patients with suspected disease recurrence were encouraged to provide blood and urine samples during follow-up visits at the cancer center. The study utilizes PredicineCARE, a targeted NGS liquid biopsy assay, to detect somatic alterations in ctDNA and to enable longitudinal monitoring of molecular recurrence.

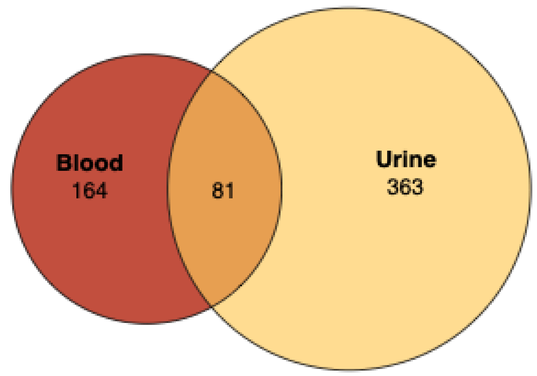
Fig. 1. Study design.



RESULTS

Overall, 132 patients with paired baseline blood and urine samples were enrolled. Including baseline and longitudinal follow-up collections, 378 samples were analyzed by the NGS assay (196 blood and 182 urine samples). At baseline, the assay detected 164 somatic mutations and 30 copy-number variations (CNVs) in blood, and 363 somatic mutations and 107 CNVs in urine. Urine samples yielded more somatic mutations than blood, with 81 mutations overlapping between the two sample types.

Fig. 2. Baseline mutation counts and overlap between blood and urine samples



At baseline, the most frequently mutated genes in urine were TP53 (30%), TERT (24%), ERBB2 (17%), CDKN2A (12%), and BRCA1 (11%). In blood, the most prevalent mutations were observed in TP53 (15%), POLE (6%), BRCA2 (5%), PIK3CG (5%), and BRCA1 (4%).

Fig. 3. The mutational landscape in baseline urine samples.

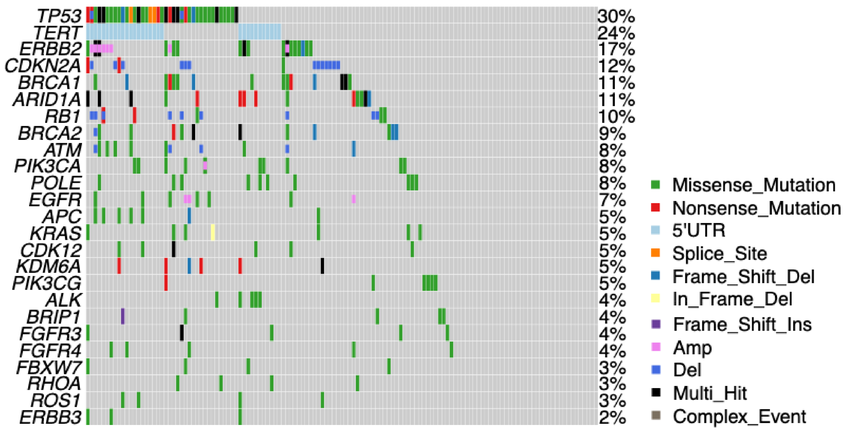
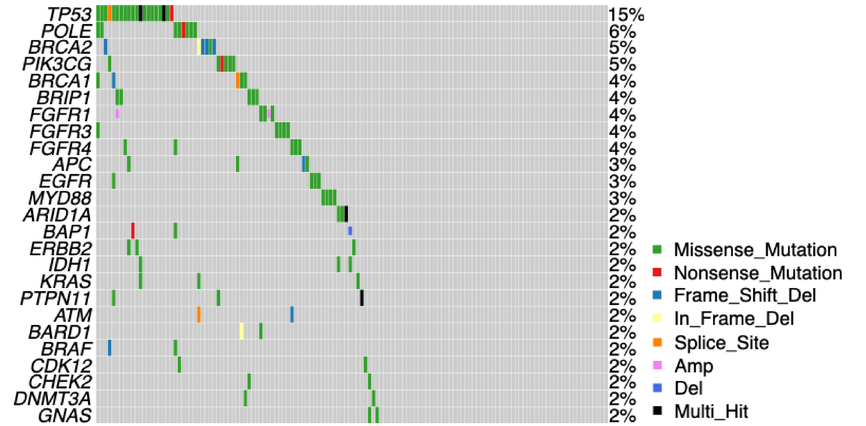
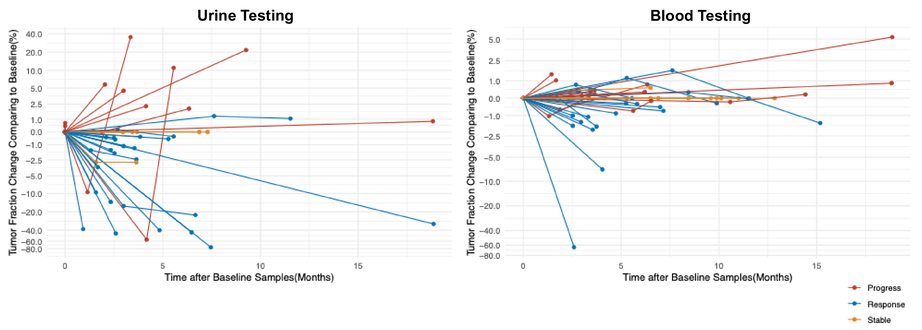


Fig. 4. The mutational landscape in baseline blood samples.



In addition, follow-up blood samples were collected from 49 patients and follow-up urine samples from 42 patients. Longitudinal molecular testing identified 17 patients with a molecular response (32 with molecular stable disease or progressive disease) in blood, and 22 patients with a molecular response (22 with molecular stable disease or progressive disease) in urine. Longer clinical follow-up is needed to confirm the relationship between these molecular findings and definitive clinical outcomes.

Fig. 5. Longitudinal tumor fraction monitoring in urine & blood samples



CONCLUSIONS

This study demonstrates the feasibility of using a targeted NGS-based liquid biopsy assay to detect and monitor ctDNA in both blood and urine of patients with bladder CIS. Urine samples showed higher sensitivity than blood, and longitudinal ctDNA dynamics correlated with clinical outcomes, supporting the potential of liquid biopsy for non-invasive disease surveillance in bladder cancer.