Abstract #: 848

Real-World Urinary Detection of FGFR Alterations to Guide FGFR Inhibitor Therapy in Bladder Cancer

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Predicine

INTRODUCTION

FGFR inhibitors have emerged as a promising therapeutic option for urothelial bladder cancer (UBC) patients harboring *FGFR* alterations (*FGFRalt*). While tissue-based testing is the gold standard for detecting *FGFRalt*, urinary tumor DNA (utDNA) analysis offers distinct advantages, including non-invasiveness and ease of sampling accessibility. Although utDNA testing has demonstrated potential in guiding clinical decision-making for *FGFR* inhibitor therapy, its implementation in real-world practice requires further evaluation to establish its reliability and utility.

METHODS

We performed longitudinal utDNA analysis on a real-world cohort of 155 UBC patients (Table 1), utilizing 322 urine samples, with the well-established PredicineCARE assay, a capture-based next-generation sequencing platform. The study aimed to evaluate the utility of utDNA in patient selection and disease monitoring.

Table 1. Patient demographics

Characteristic	Category	Value (N=155)
Age (years)		
	Mean ± SD	65.9 ± 9.7
	Median (Range)	66 (36 – 90)
Gender		
	Male	129 (83.2%)
	Female	26 (16.8%)
UBC subtype		
	MIBC	78 (50.3%)
	NMIBC	77 (49.7%)
Tumor Stage (T)		
	Ta	26 (16.8%)
	T1	51 (32.9%)
	T2	60 (38.7%)
	T3	18 (11.6%)
Nodal Stage (N)	N0	155 (100.0%)
Metastasis (M)	M0	155 (100.0%)
Histological Grade		
	High Grade	147 (94.8%)
	Low Grade	8 (5.2%)
Prior Treatment		
	BCG (Yes)	38 (24.5%)
	Chemotherapy (Yes)	50 (32.3%)
	Immunotherapy (Yes)	22 (14.2%)

MIBC, Muscle-Invasive Bladder Cancer; NMIBC, Non-Muscle-Invasive Bladder Cancer; BCG, Bacillus Calmette-Guérin

RESULTS

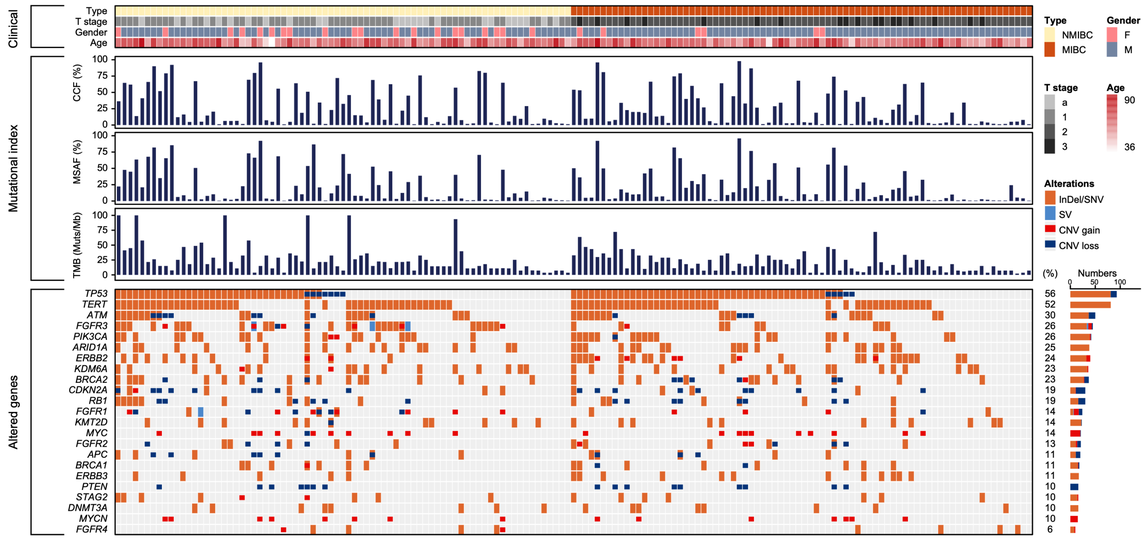

Fig 1. Genomic Landscape and Clinicopathological Features of Urothelial Bladder Cancer (N=155). Each column represents an individual patient, while rows represent specific clinical or genomic alterations detected in utDNA. The top panel indicates key clinicopathological features. The middle panel illustrates quantitative mutational indices, including cancer cell fraction (CCF), maximum somatic mutation allele frequency (MSAF), and tumor mutation burden (TMB). The bottom panel displays specific somatic genomic alterations, with genes ordered by mutation frequency. The most frequently altered genes in this cohort are *TP53* (56%), *TERT* (52%), *FGFR3* (30%), *PIK3CA* (26%), and *ARID1A* (26%).

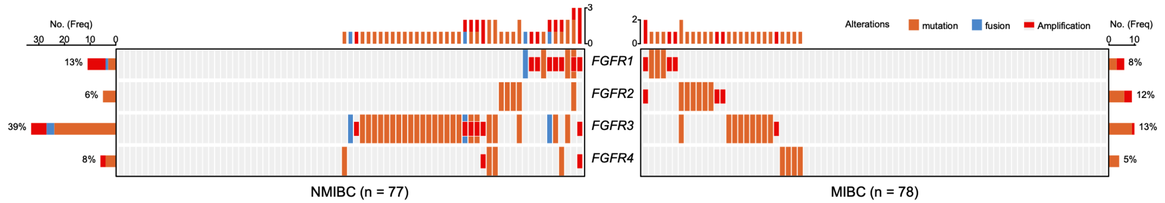

Fig 2. Comparison of FGFR Family Genomic Alterations in NMIBC and MIBC Cohorts. Oncoprint display of somatic alterations in FGFR1, FGFR2, FGFR3, and FGFR4 across patients with Non-Muscle Invasive Bladder Cancer (NMIBC, n=77) and Muscle-Invasive Bladder Cancer (MIBC, n=78). Each column represents an individual patient sample. The prevalence of FGFR3 alterations is significantly higher in the NMIBC cohort (39%) compared to the MIBC cohort (13%) (Fisher's exact test, $p < 0.001$).

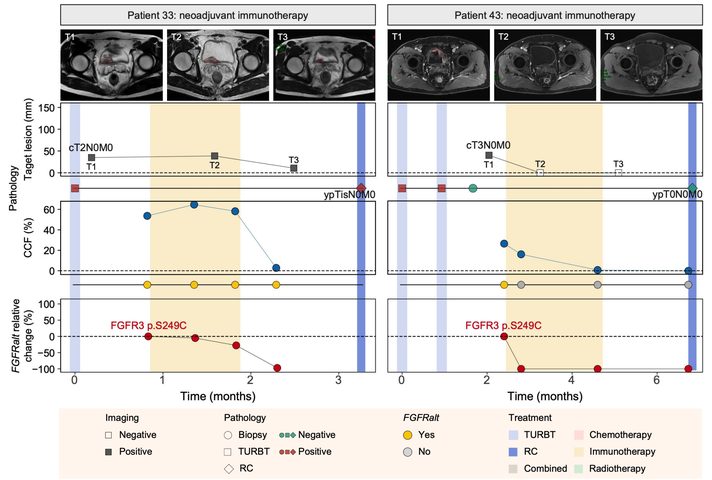

Fig 3. utDNA monitoring for patients under neoadjuvant immunotherapy. Both patients (Patient 33 and 43) showed a reduction in CCF and FGFR mutation allele frequency, which directly correlates with the clinical evaluation by CT imaging and final pathology review.

CONCLUSIONS

Urinary tumor DNA (utDNA) effectively captures the diverse mutational landscape of both Non-Muscle Invasive (NMIBC) and Muscle-Invasive Bladder Cancer (MIBC). The PredicineCARE utDNA assay provides a non-invasive means to profile critical driver genes—including FGFR3, ERBB2, and PIK3CA—offering a robust platform for patient selection for targeted therapies. Furthermore, utDNA dynamics offer a sensitive method for longitudinal disease monitoring. Tracking changes in the Cancer Cell Fraction (CCF) and specific driver allele frequencies (e.g., FGFR alterations) allows for the real-time assessment of treatment response, potentially enabling more agile clinical decision-making during neoadjuvant or systemic therapy.