Describing the genomic landscape of bladder cancer histologic subtypes

Abstract No.: 680

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INTRODUCTION

- **Histologic subtypes of bladder cancer are associated with poor prognosis and therapy resistance**
- **Understanding underlining biology can help identify biomarkers and therapeutic targets**
- **In this study, we aim to describe the genomic alteration (GA) landscape of pure urothelial (UC) & histologic subtypes: plasmacytoid (PC), micropapillary (MP), sarcomatoid (SA), small cell/neuroendocrine (SC), squamous cell differentiation (SQ), adenocarcinoma (AD).**

METHODS

Patients with Bladder Cancer N = 2,065 → Molecular profiling with Tempus assays*

Study Criteria:

- Diagnosis of bladder cancer (UC or histologic subtypes: PC, MP, SA, SC, SQ, AD)

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Retrospective analysis

Genomic and immunotherapy putative biomarkers, including mutations, fusions, copy number variants, tumor mutation burden (TMB-high defined as ≥10 mutations/Mb) and MSI status were determined for each subtype and compared using Fisher's Exact and Kruskal-Wallis tests.

*Briefly, Tempus xT is a targeted, tumor/normal-matched DNA panel that detects single-nucleotide variants (SNVs), insertions and/or deletions (indels), and copy number variants (CNVs) in 648 genes, as well as chromosomal rearrangements in 22 genes with high sensitivity and specificity

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SIGNIFICANCE

- **Distinct genomic alteration patterns were found among different histologic subtypes of bladder cancer & conventional UC.**
- **Assessing the genomic landscape of bladder cancer can help identify potential 'actionable' targets & biomarkers, and better inform clinical trial designs, therapies & eligibility, including "basket" or "umbrella" trials.**
- **MP, SA, SQ subtypes have higher prevalences (>10%) of FGFR2/3 alterations.**

RESULTS

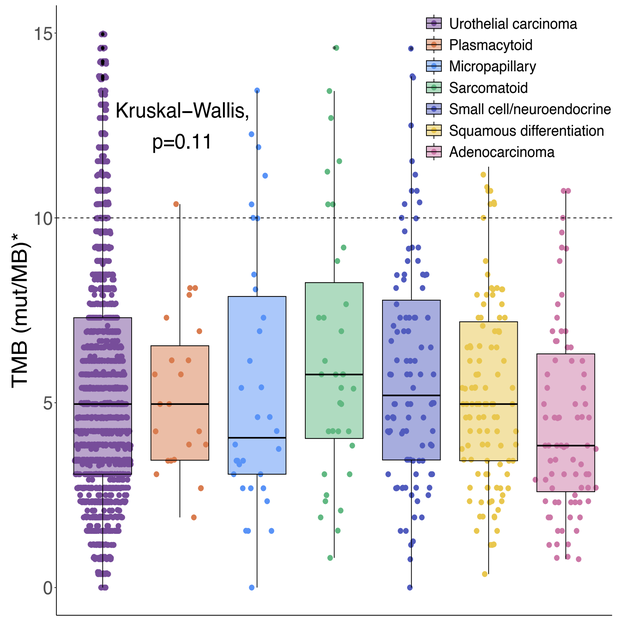
Table 1. Cohort Demographics

Characteristic	Overall N = 2,165[1]	UC N = 1,738[1]	PC N = 25[1]	MP N = 38[1]	SA N = 37[1]	SC N = 113[1]	SQ N = 126[1]	AD N = 88[1]	p-value[2]
Age at Diagnosis									<0.001
Median (IQR)	70 (62, 77)	70 (62, 77)	65 (60, 74)	65 (60, 74)	71 (67, 79)	71 (64, 77)	67 (58, 75)	67 (58, 74)	
Range	26, 90	26, 90	45, 89	36, 89	45, 90	31, 90	33, 90	31, 88	
Unknown	17	11	2	1	0	1	1	1	
Gender									<0.001
Male	1,578 (73%)	1,303 (75%)	18 (72%)	27 (71%)	25 (68%)	86 (76%)	59 (47%)	60 (68%)	
Female	587 (27%)	435 (25%)	7 (28%)	11 (29%)	12 (32%)	27 (24%)	67 (53%)	28 (32%)	
Race/Ethnicity									0.009
White	1,171 (84%)	942 (84%)	11 (85%)	22 (85%)	26 (96%)	63 (90%)	73 (81%)	34 (63%)	
Black or African American	112 (8.0%)	83 (7.4%)	2 (15%)	1 (3.8%)	1 (3.7%)	5 (7.1%)	9 (10%)	11 (20%)	
Other	76 (5.4%)	61 (5.5%)	0 (0%)	3 (12%)	0 (0%)	1 (1.4%)	8 (8.9%)	3 (5.6%)	
Asian	40 (2.9%)	33 (2.9%)	0 (0%)	0 (0%)	0 (0%)	1 (1.4%)	0 (0%)	6 (11%)	
Hispanic or Latino	48 (6.3%)	39 (6.4%)	0 (0%)	0 (0%)	0 (0%)	4 (8.9%)	1 (2.4%)	4 (14%)	
Smoker status									0.005
Current/former smoker	1,222 (71%)	1,001 (73%)	15 (68%)	22 (71%)	24 (80%)	55 (60%)	66 (61%)	39 (57%)	
Never smoker	503 (29%)	373 (27%)	7 (32%)	9 (29%)	6 (20%)	36 (40%)	42 (39%)	30 (43%)	
Unknown	440	364	3	7	7	22	18	19	

[1] n (%), [2]Kruskal-Wallis rank sum test; Fisher's Exact Test for Count Data

Table 1. Among 2165 identified pts, 1738 (80%) had UC (84% pure and 16% mixed histology), Table shows genomic alterations per histologic subtype. Of 1197 pts with staging information available, 71% tumors were stage IV.

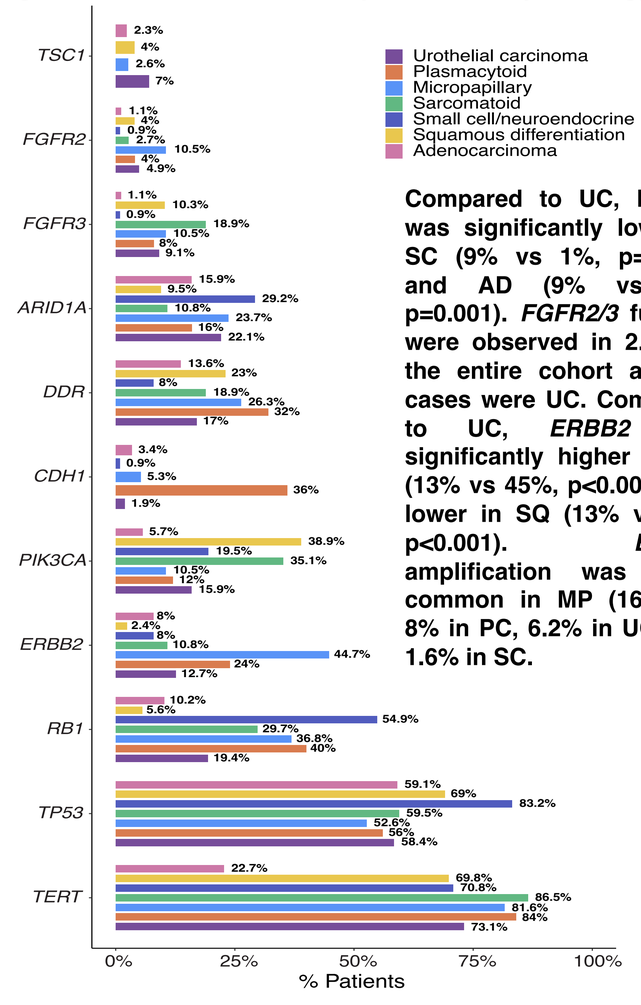
Figure 1. TMB Stratified By Histology



*y–axis truncated at 15. Dashed line indicates cutoff for High

Figure 1. TMB-H status were noted in 17% of the overall cohort and was relatively similar across histologies.

Figure 2. Somatic GAs Landscape Stratified By Histology



Compared to UC, FGFR3 was significantly lower in SC (9% vs 1%, p=0.003) and AD (9% vs 1%, p=0.001). *FGFR2/3* fusions were observed in 2.6% of the entire cohort and all cases were UC. Compared to UC, *ERBB2* was significantly higher in MP (13% vs 45%, p<0.001) and lower in SQ (13% vs 2%, p<0.001). *ERBB2* amplification was more common in MP (16%) vs 8% in PC, 6.2% in UC, and 1.6% in SC.