



Memorial Sloan Kettering
Cancer Center

Genomic Predictors of Pathological Upstaging of Clinically Localized Urothelial Carcinoma at Radical Cystectomy (MP55-03)

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Introduction

- Use of neoadjuvant (NAC) remains low despite level 1 evidence
- Upstaging of cT1-2 to non-organ confined pathological stage \geq T3 or N+ at radical cystectomy (RC) is common
- Prior studies, including TCGA, have demonstrated that luminal tumors are associated with lower rates of pathologic upstaging at RC^{1,2}
- Given luminal tumors are enriched with *FGFR3* alterations, we sought to identify genomic predictors of upstaging

Table 2 – Rates of upstaging for luminal versus nonluminal (basal, claudin low, and infiltrated luminal) tumors in clinical T1/T2 patients from the upstaging cohort

Variables	Luminal	Nonluminal	p value
Total, n (%)	100 (48)	106 (52)	
Upstaging (\geq pT3 and/or pTanyN+), n (%)			
No	66 (66)	52 (49)	0.02
Yes	34 (34)	54 (51)	

Table 5 – Rates of upstaging for luminal versus nonluminal (basal, claudin low, and infiltrated luminal) tumors in clinical T1/T2 patients from the TCGA cohort

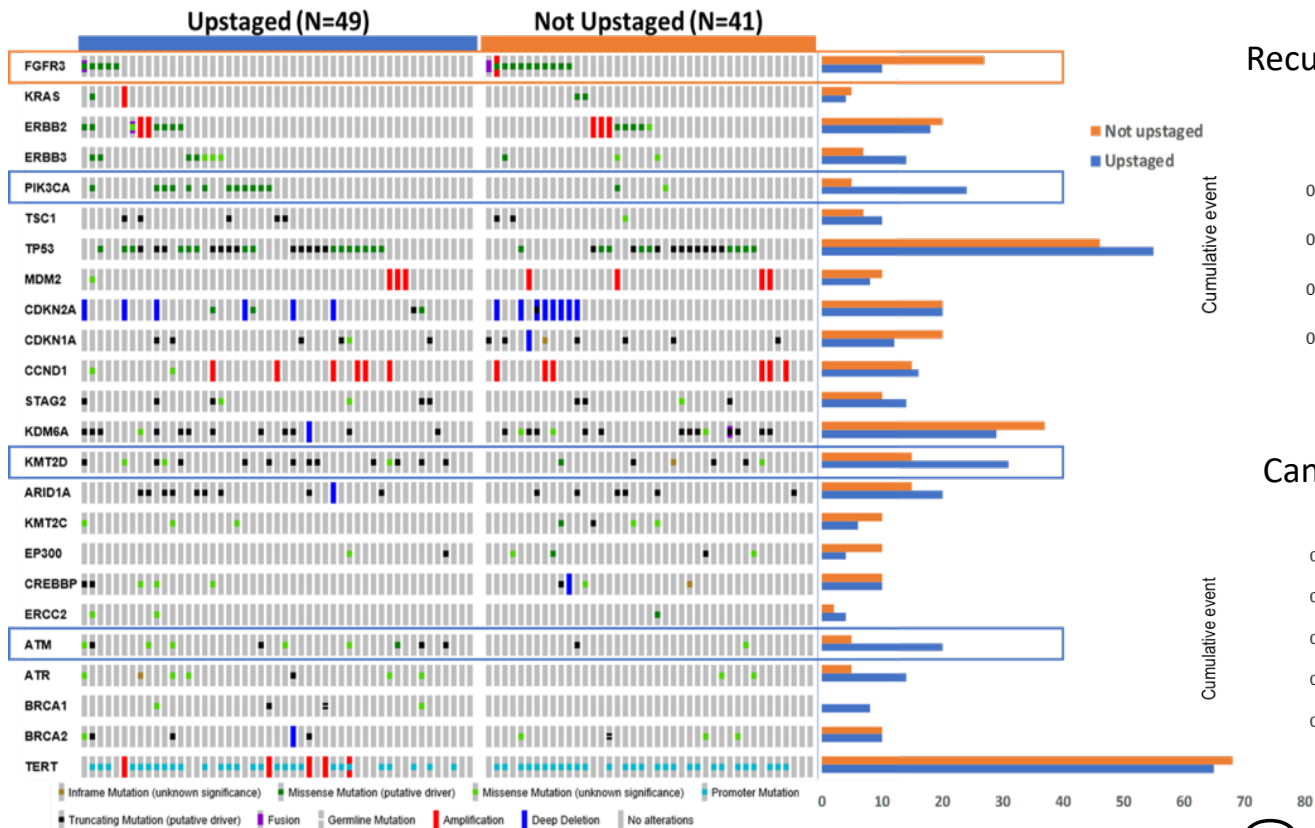
Variables	Luminal	Nonluminal	p value
Total, n (%)	22 (23)	74 (77)	
Upstaging (\geq pT3 and/or pTanyN+), n (%)			
No	12 (55)	20 (27)	0.006
Yes	6 (27)	48 (65)	
Unavailable	4 (18)	6 (8.1)	

¹ Lotan et al. Eur Urol.76(2019):200-6.

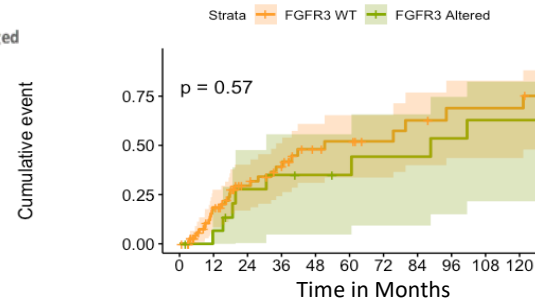
² Robertson et al. Cell.171(2017):540-56.



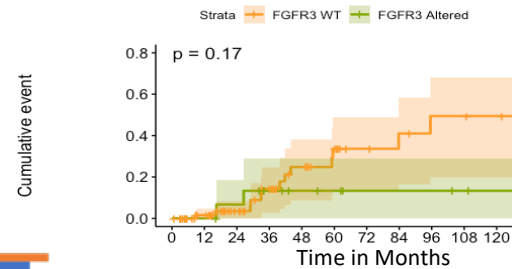
MSK-IMPACT of Upstaged vs Not Upstaged at RC



Recurrence-Free Survival



Cancer-Specific Survival



Conclusions

- Despite the low use of NAC, there remains a **majority** of patients who would benefit given high rate of upstaging
- In a selected cohort of patients without NAC, we have identified multiple genomic predictors of upstaging
- Utilizing our prospective efforts, we will provide validation of genes like *PIK3CA*, *KDM2D* and *ATM* are more likely to harbor non-organ confined disease
- Use of genomic predictors should provide a biomarker to **increase** the utilization of NAC

