Molecular Characteristics of Advanced clear cell Renal Cell Carcinoma (ccRCC) Harboring *TERT* Mutations

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ASCO Genitourinary Cancers Symposium

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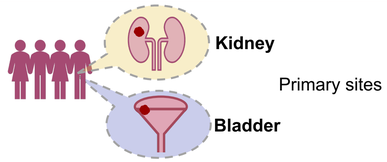
INTRODUCTION



- TERT is a catalytic subunit of the telomerase enzyme
- *TERT* promoter mutations lead to increased telomerase activity, which promotes tumorigenesis by preventing telomere shortening
- Emerging data suggests a correlation between *TERT* promoter mutations and improved responses to immune checkpoint inhibitors in urothelial carcinoma (UC) but the role in RCC is unknown

This study aims to analyze the immune biomarker environment and co-mutational landscape in *TERT* mutated versus wildtype in RCC and UC

METHODS

Advanced ccRCC (N=866) /UC (N=2580) Patients + Molecular profiling with Tempus xT assay*

Retrospective review of De-identified patient data

Analyses performed

***TERT* Other** = Other pathogenic mutations	***TERT* Promoter** = 124 C>T	Wildtype = ***TERT* wt**

Companion alterations and immune biomarkers were compared between these three groups

*Tempus xT assay - DNA-seq of 648 genes at 500x coverage, full transcriptome RNA-seq

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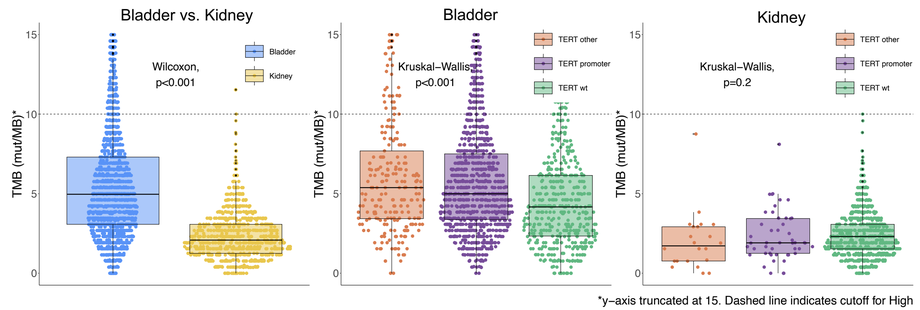
SUMMARY

- This is the **largest analysis** of the molecular and immune landscape of ***TERT* mutated ccRCC**
- This dataset showcases that traditional immune biomarkers (i.e. TMB and PD-L1) **do not appear to be highly prevalent in RCC compared to UC** and their use in clinical practice may be limited.
- Our UC dataset displays similar trends as previously published that *TERT* altered tumors are associated with higher immune biomarker expression than *TERT* wt. Further investigation into the *TERT* biomarker candidate is warranted

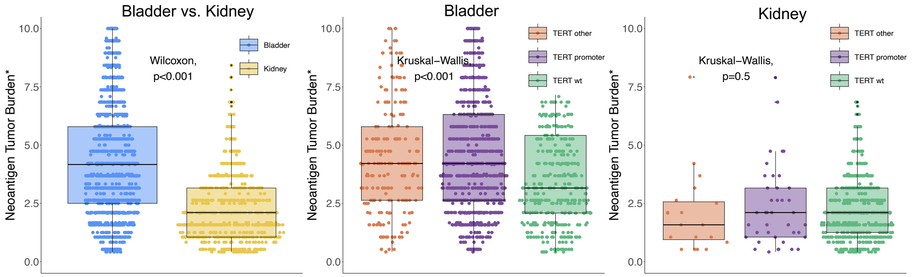
RESULTS

Figure 1 – Tumor mutational burden in UC versus RCC cohorts and in *TERT* altered versus wt tumors. Note, TMB of bladder cohort is greater than Kidney's.



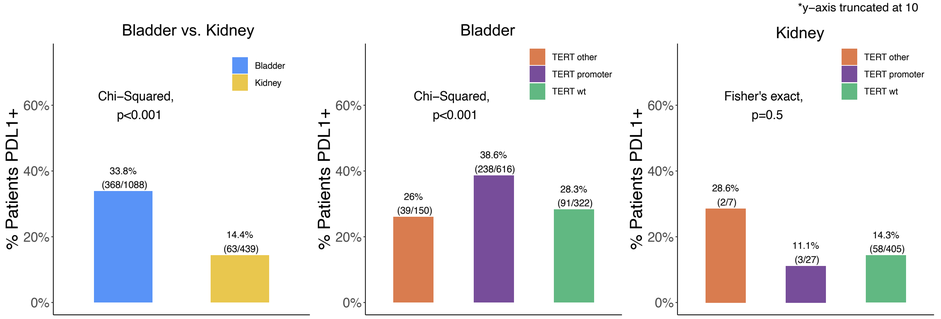
*y–axis truncated at 15. Dashed line indicates cutoff for High

Figure 2 – Neoantigen tumor burden in UC versus RCC cohorts and in *TERT* altered versus wt tumors. Note, Neoantigen Tumor burden of bladder cohort is greater than Kidney's.



*y–axis truncated at 10

Figure 3 – PD-L1 in UC versus RCC cohorts and in *TERT* altered versus wt tumors. Note, more %PDL1+ pts in Bladder cohort versus kidney.



PDL1+= Programmed Death Ligand 1 - Positive

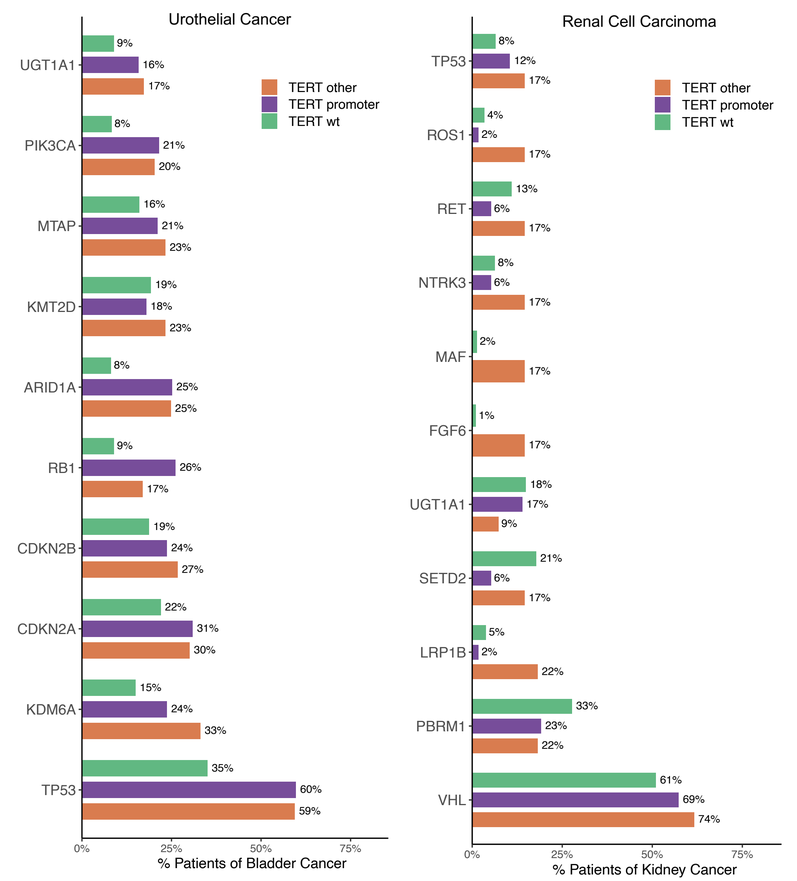


Figure 4 - Distribution of co-alterations in *TERT* altered and wt tumors in UC and RCC cohorts