Matched Tissue and circulating tumor DNA (ctDNA) Analysis in Renal Cell Carcinoma (RCC): Results from a multimodal real-world database

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INTRODUCTION

Next generation sequencing (NGS) of ctDNA can complement tissue NGS and is a non-invasive test that can be conducted serially, with the potential to enhance assessment of spatial and temporal molecular tumor heterogeneity. Here, we investigated mutations in RCC patients from matched tissue and ctDNA genomic profiling.

METHODS

- From the Tempus multimodal database, we retrospectively analyzed de-identified NGS data from patients (pts) with RCC that had dual tissue (Tempus xT, 648 genes) and ctDNA testing (Tempus xF, 105 genes)
- Pts with matched samples (collected +/- 90 days of one another) were included
- Clinical characteristics and select pathogenic somatic short variants (PSSV) and copy number variants [(amplifications and deletions, two copy number losses (CNL)] were evaluated.
- Concordance analyses were restricted to the 105 genes tested on the ctDNA panel and further restricted to short variants, with the exception of amplifications and CNL detected by both xF and xT.

Characteristic	N = 393
Age at Diagnosis	
Median (IQR)	61 (52, 68)
Range	19, 89
Unknown	21
Gender	
Male	280 (71%)
Female	113 (29%)
Race	
White	187 (75%)
Black or African American	31 (12%)
Other Race	20 (8.0%)
Asian	12 (4.8%)
Unknown	143
Ethnicity	
Not Hispanic or Latino	141 (80%)
Hispanic or Latino	36 (20%)
Unknown	216
Smoking Status	
Never smoker	174 (57%)
Current/former smoker	133 (43%)
Unknown	86
Time from Tissue Collection to Liquid (Days)	
Median (IQR)	21 (7, 39)
Range	-63, 90

Table 1. Patient clinical and demographic characteristics.

SUMMARY

- ctDNA profiling is complementary to tissue based NGS in RCC and can increase the detection of genomic alterations.
- Concordance between ctDNA and tissue profiling was higher in individuals with metastatic disease.
- Future research is warranted to understand how longitudinal ctDNA analysis can define biomarkers of response and resistance at the mutation and ctDNA fraction levels.

RESULTS

Breakdown of sample biopsy site

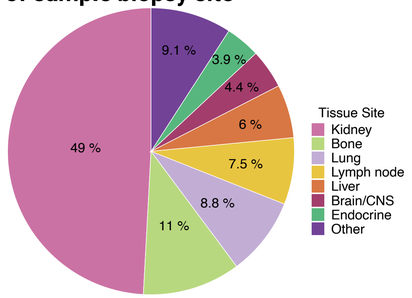

Figure 1. Biopsies were collected from primary and metastatic sites. 8 patients had unknown status; Endocrine is defined as pancreas, adrenal gland, and thyroid. Other is defined as soft tissue, urinary tract, GI tract, peritoneum, and pleura.

The combination of tissue and ctDNA testing increased detection of genomic alterations

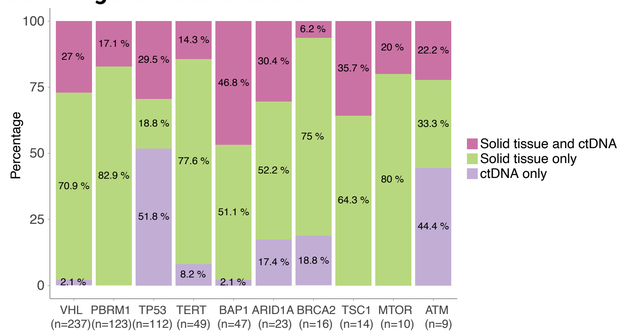

Figure 3. For all samples and all relevant alterations indicated, we assessed the fraction that were detected by both Tempus xT and Tempus xF (concordant), as well as those detected solely by either Tempus xT or Tempus xF.

Prevalence of molecular alterations detected according to solid-tissue (xT) and ctDNA testing (xF)

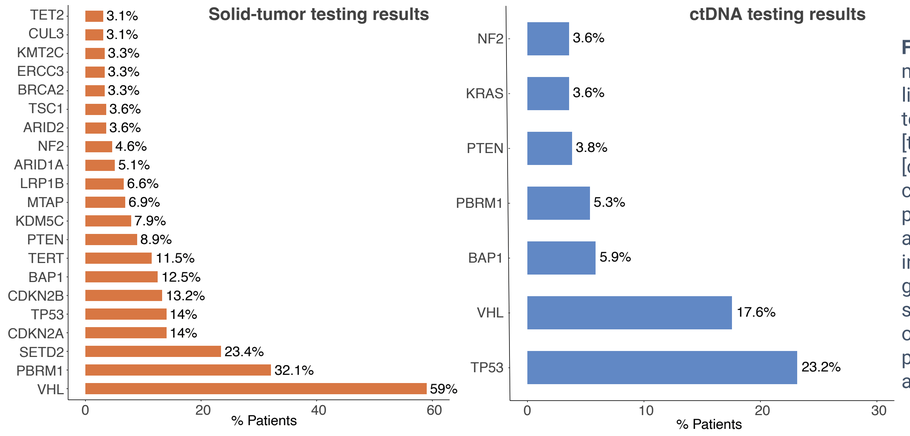

Figure 2. Genes harboring the most common alterations are listed for their respective testing platform (Tempus xT [tissue] and Tempus xF [ctDNA]). Both tissue and ctDNA testing identified potentially targetable alterations. Genomic alterations included in the respective graphs may have been detected solely by the indicated modality or by both modalities (n=393 patients for both Tempus xT and Tempus xF).

Concordance between solid-tissue and ctDNA results is higher in metastatic disease

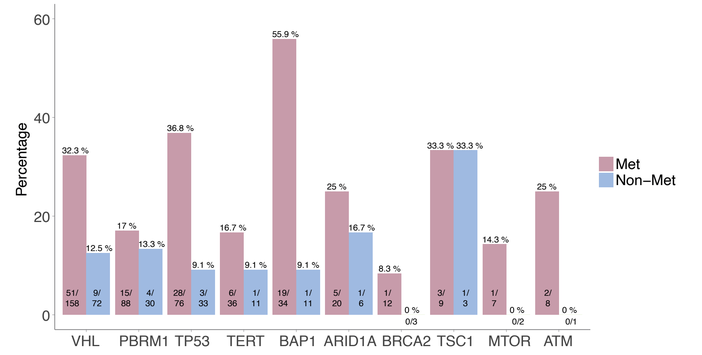

Figure 4. After stratifying samples according to metastatic status (n=260 [metastatic] and n=120 [non-metastatic]), we assessed the percentage of concordant variants (*e.g.,* detected by both Tempus xT and Tempus xF) out of all variants (detected by *either* Tempus xT, Tempus xF, or both) for individual genes. Metastatic status was categorized based off of status listed prior to sample collection for *both* Tempus xT and Tempus xF, note that 13 patients were excluded from this analysis due to possibly conflicting metastatic diagnoses. The numerator and denominator for all percentages in the graph are listed within or below the relevant bars.

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