KCRS 24 Kidney Cancer Research Summit

Concordance Analysis of Tissue and ctDNA in RCC: Insights from a Multimodal Real-World Database

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Background

EXCLUSION ZONE

Next generation sequencing (NGS) of ctDNA can complement tissue NGS and is a non-invasive test that can be conducted serially.

Its application enhances the assessment of spatial and temporal molecular tumor heterogeneity, providing insights into progression and treatment response.

However, limited studies have been conducted in RCC.

Aim: Investigate molecular alterations detected in circulating and tissue-derived DNA in patients with RCC.

Methods

EXCLUSION ZONE

Retrospective analysis of de-identified NGS data from patients with RCC that had both tissue (xT, 648 genes) and ctDNA testing (xF, 105 genes). [Tempus multimodal database]

Inclusion: Patients with matched samples (collected +/- 90 days of one another) and diagnosis of RCC

Analysis: Socio-demographic and clinical characteristics and select pathogenic somatic short variants (PSSV) and copy number variants [(amplifications and deletions, two copy number losses (CNL)].

Concordance analysis: 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.

Subgroup analysis: Based on the presence and absence of metastasis

Results

EXCLUSION ZONE

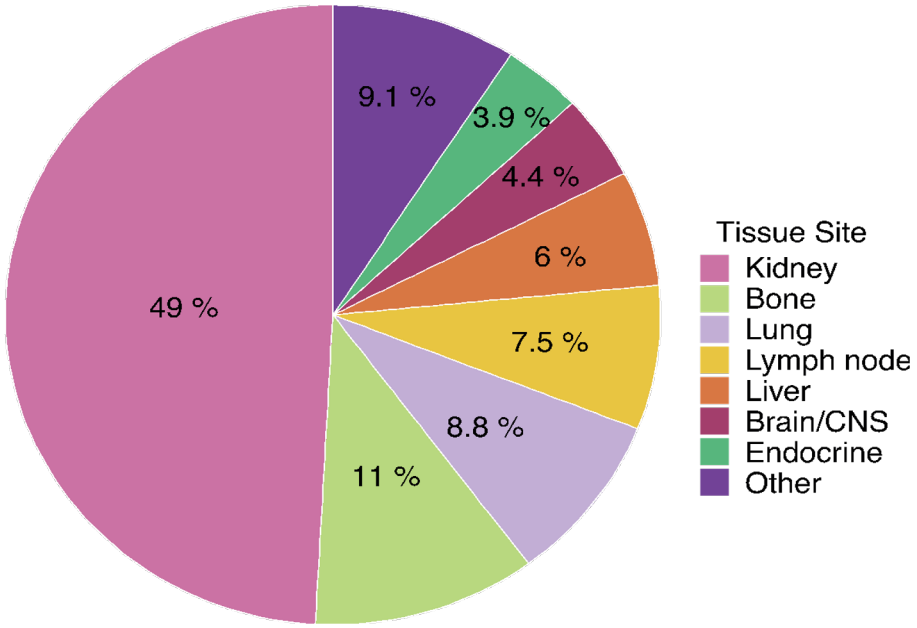


Figure 1: Breakdown of tissue biopsy site

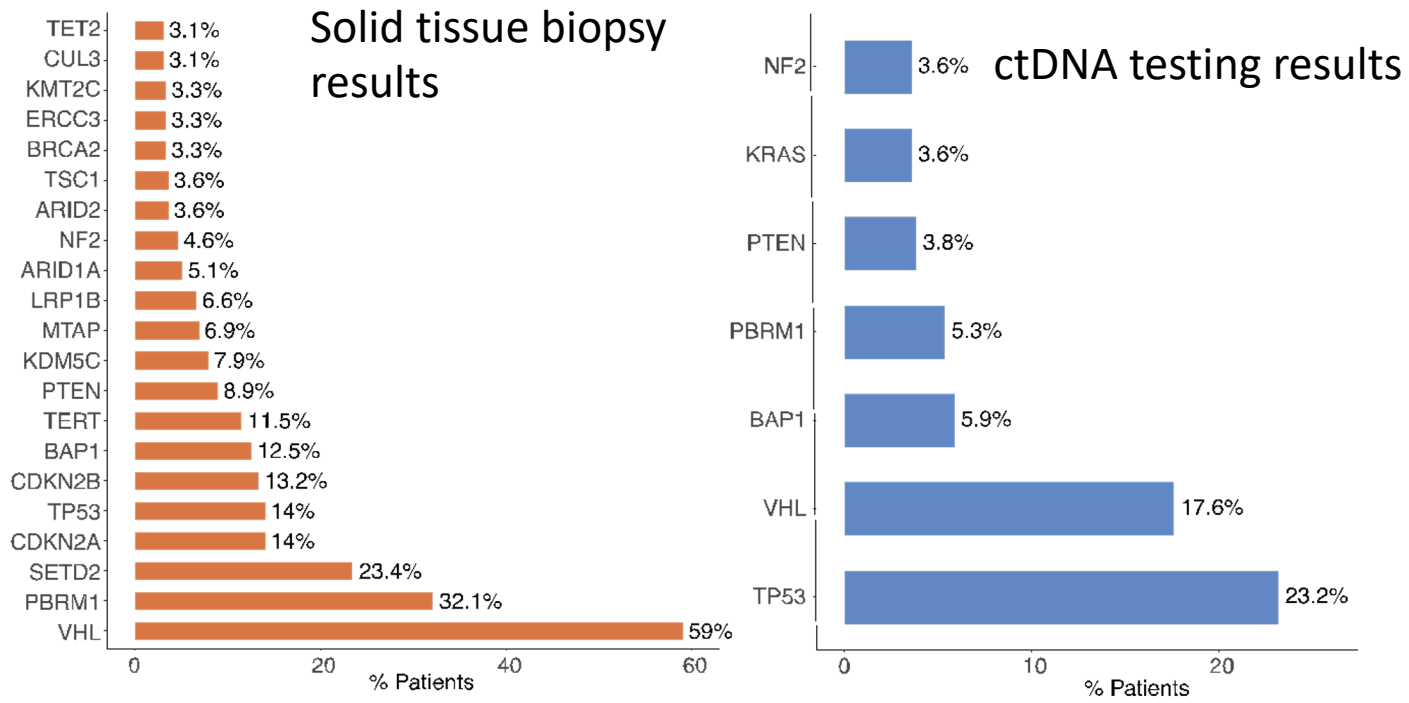
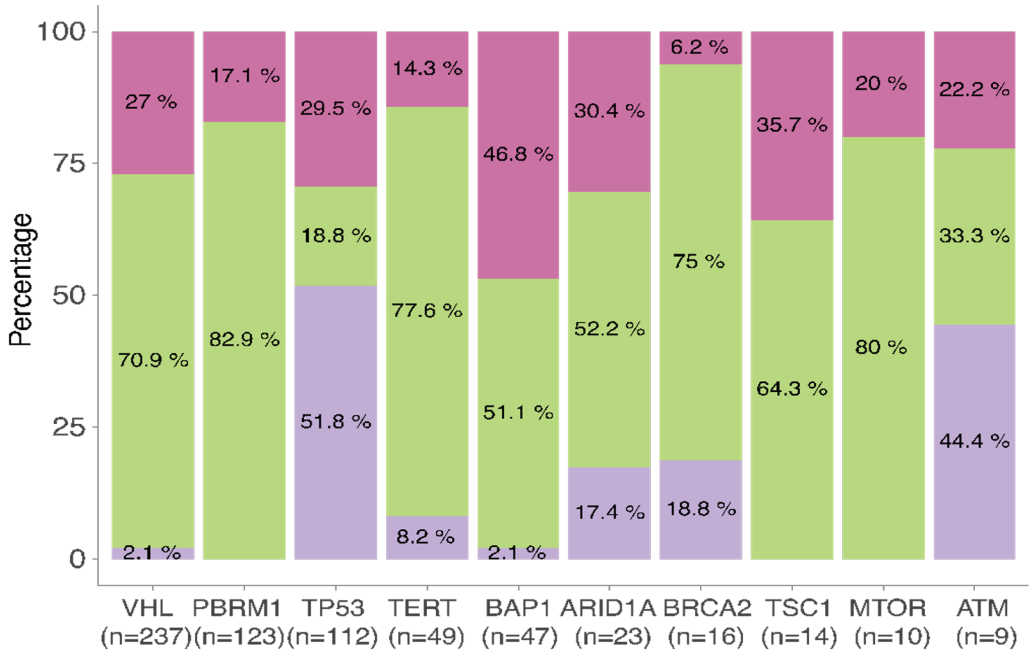


Figure 2: Prevalence of molecular alterations detected according to solid-tissue and ctDNA testing.

Results

EXCLUSION ZONE



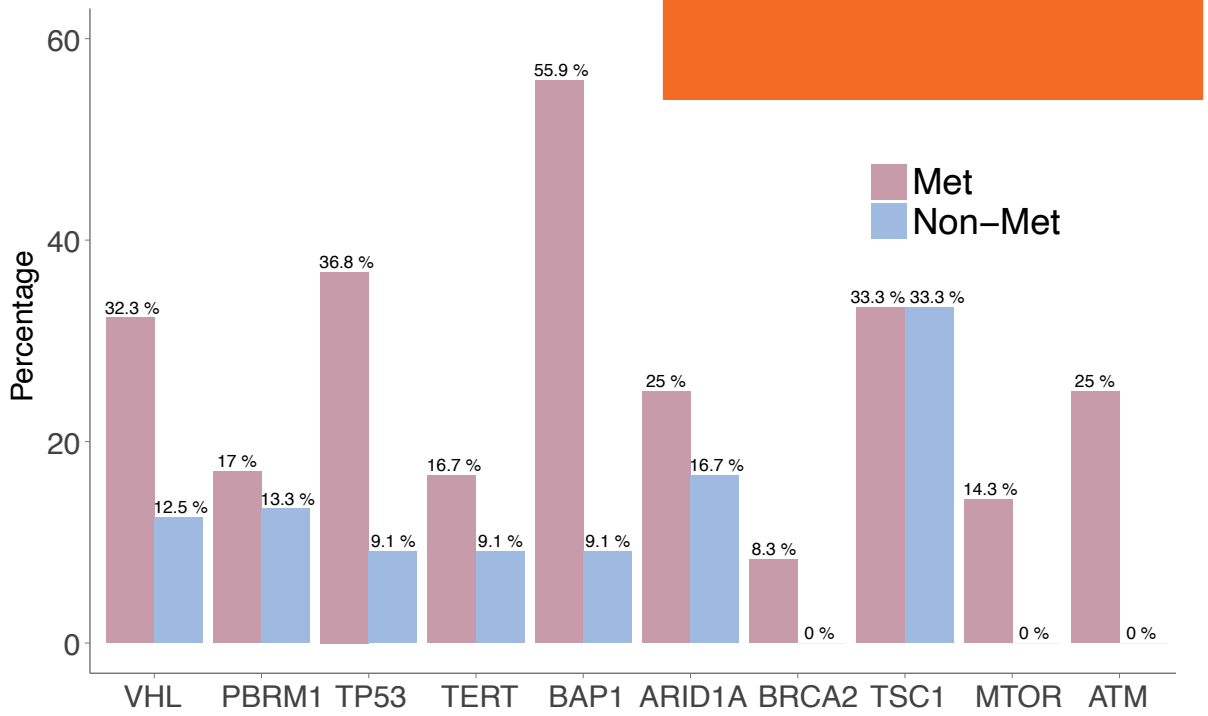


Figure 3: Breakdown of alterations according to assay detection type, including assay unique alterations and those detected by both assays.

Solid tissue and cfDNA
Solid tissue only
cfDNA only

Figure 4: Concordant alterations identified in solid tissue and ctDNA (stratified based on metastasis)

Summary & Conclusion

EXCLUSION ZONE

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, suggesting a potential utility in advanced stages of RCC.

Further research is warranted to elucidate how longitudinal ctDNA analysis can delineate biomarkers of response and resistance at both the mutation and ctDNA fraction levels.

Understanding these dynamics could offer valuable insights into disease progression and guide personalized treatment strategies for RCC patients.