Dual tissue and plasma testing improves detection of actionable variants in patients with solid cancers

Abstract #: 3017

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INTRODUCTION

Next generation sequencing (NGS) of tumor tissue and plasma (circulating tumor DNA [ctDNA]) are used clinically to identify actionable genomic alterations, with implications for treatment selection and disease surveillance. Early studies have observed that solid tumor tissue and ctDNA testing may capture both overlapping and complementary alterations. Using the Tempus Lens database, we examined whether patients tested with **both tissue and ctDNA**, **"dual testing"**, improved identification of actionable variants compared with either modality alone. In particular, we focused on the actionable findings identified by ctDNA testing in addition to solid tumor testing standard of care.

METHODS

We retrospectively analyzed 3153 de-identified stage 4 patients across four cancer types (Table 1). Each patient had dual testing which resulted in clinical reports for both tests—Tempus xF (ctDNA) and Tempus xT (solid tissue)**.** Patients were stratified into concurrent or longitudinal cohorts (Figure 2).

All analyses were limited to variants that met the limit-of-detection criteria for both assays (104 genes). **Actionability was defined as indication-matched somatic variants with OncoKB Level 1 and 2 evidence, and somatic or germline variants with OncoKB Level R1 evidence.**[1] SNVs, insertions, and deletions (14 genes), fusions (4 genes), copy number variants (2 genes), and microsatellite instability were all included for analysis.

Cancer type	Concurrent Patients: Actionable (Total)	Longitudinal Patients: Actionable (Total)	Patient sex (% Female)	Age in years at 1st collection (median)
Breast (n=644)	187 (380)	96 (264)	99	60
Colorectal (n=841)	308 (485)	213 (356)	44	61
NSCLC (n=1232)	374 (969)	93 (263)	52	67
Prostate (n=436)	29 (215)	15 (221)	0	67
Pan cancer (n=3153)	898 (2049)	417 (1104)	51	65

Table 1. Overview of patient population.

SUMMARY

Of 1,315 patients with actionable findings identified via **dual testing**:

- **ctDNA testing identified** actionable variants **missed by solid tumor** testing in **9% of patients**.
- ctDNA identified actionable variants missed by solid tumor testing in both concurrent and longitudinal cohorts across cancer types

RESULTS

Dual testing identifies more patients with actionable findings than single modality testing alone

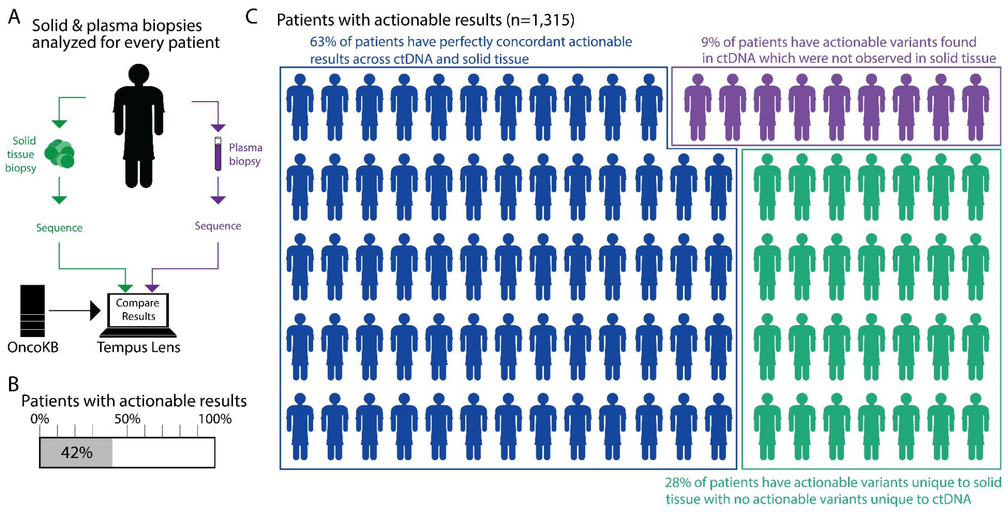

Figure 1. (A) Overview of study design. (B) All patients with actionable variants (n=1,315). (C) Breakdown of all patients with actionable variants identified by both (blue) or individual assays (purple and green).

Dual testing increases identification of patients with actionable findings across cancer types

Figure 3. The percentage of patients with actionable findings identified by ctDNA testing that would be missed by solid tumor testing alone stratified by cancer type and cohort: concurrent (dark purple); longitudinal (light purple) .

Dual testing increases identification of patients with actionable findings in both concurrent and longitudinal settings

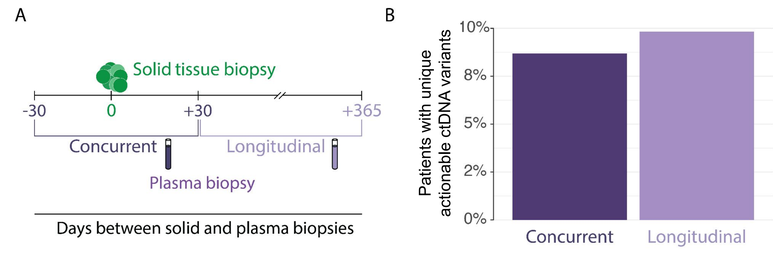

Figure 2. (A) Definition of cohorts, all days are in reference to solid tissue biopsy date. Median absolute time between biopsies are 11 days (IQR 6-17) and 96 days (IQR 47-197) for concurrent and longitudinal cohorts, respectively. (B) The percentage of patients with actionable findings identified by ctDNA that would have been missed by solid tumor testing alone.

Concurrent dual testing identifies targetable and resistant variants missed by solid tissue profiling

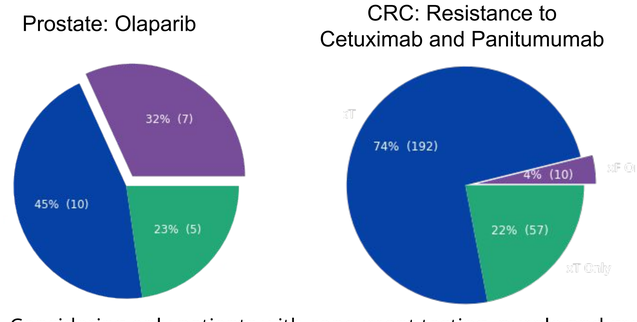

Figure 4. Considering only patients with concurrent testing, purple and green wedges show the percentage of patients matched to each drug that were identified by ctDNA and solid tissue testing, respectively, and would have been otherwise missed with single modality testing. The percentage of patients that were identified by both assays is shown in blue.

Affiliations

1. OncoKB Level 1 is defined as an FDA-recognized biomarker predictive of response to an FDA-approved drug in the specified indication. OncoKB Level 2 is defined as a standard care biomarker recommended by the NCCN or other professional guidelines predictive of response to an FDA-approved drug in the specified indication. OncoKB Level R1 is defined as a standard care biomarker predictive of resistance to an FDA-approved drug in the relevant indication.