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

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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.

SUMMARY

Of 1,315 patients with actionable variants 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

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

Affiliations

TEMPUS

VANDERBILT UNIVERSITY MEDICAL CENTER

THE OHIO STATE UNIVERSITY COMPREHENSIVE CANCER CENTER

Washington University in St. Louis, MO

TriHealth Cancer Institute, Cincinnati, OH

MainHealth Cancer Care, South Portland, ME

St. Luke’s Cancer Institute, Kansas City, MO

The Ohio State University, Columbus, OH

Vanderbilt University Medical Center, Nashville, TN

Table 1. Overview of patient population.

<table>
<thead>
<tr>
<th>Cancer type</th>
<th>Concurrent Patients: Actionable (Total)</th>
<th>Longitudinal Patients: Actionable (Total)</th>
<th>Patient sex (% Female)</th>
<th>Age in years at 1st collection (median)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>187 (380)</td>
<td>96 (264)</td>
<td>99</td>
<td>60</td>
</tr>
<tr>
<td>Colorectal</td>
<td>308 (485)</td>
<td>213 (356)</td>
<td>44</td>
<td>61</td>
</tr>
<tr>
<td>NSCLC</td>
<td>374 (969)</td>
<td>93 (263)</td>
<td>52</td>
<td>67</td>
</tr>
<tr>
<td>Prostate</td>
<td>29 (215)</td>
<td>15 (221)</td>
<td>0</td>
<td>67</td>
</tr>
<tr>
<td>Pan cancer</td>
<td>898 (2049)</td>
<td>417 (1104)</td>
<td>51</td>
<td>65</td>
</tr>
</tbody>
</table>

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 NCI 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 specified indication.