Relationship Between Dynamic Changes in Circulating Tumor Fraction and Real-World imaging with Real-World Survival in Patients with Solid Tumors Treated with Immunotherapy

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INTRODUCTION

- There is an unmet need for a sensitive biomarker that can determine which patients will derive long term benefit from immune checkpoint inhibitors (ICI)
- While radiologic imaging is the current standard of care for assessing ICI response, imaging can be difficult to interpret and is typically only assessed at fixed intervals
- Dynamic changes in circulating tumor fraction (TF) is a potential biomarker for monitoring ICI response
- Here, we show the clinical benefit of a molecular biomarker, xM for treatment response monitoring (TRM), both alone and in combination with imaging, in a real-world (rw), pan-cancer cohort treated with ICIs

METHODS

- Using the Tempus liquid biopsy assay, ctDNA TF was computed by applying an ensemble algorithm incorporating copy number variant data and pathogenic variant allele frequencies
- De-identified patient records from the Tempus multimodal database were analyzed if patients had a baseline xF test ≤ 40 days (median=13 days) prior to the ICI start (alone or with chemotherapy) and an on-treatment xF test 15-180 days (median=93 days) post-ICI start. Additionally, patients that terminated ICI and had an on-treatment xF test within 40 days of ending their ICI therapy were also considered evaluable
- Patients had imaging 15-126 days (median=77 days) post-ICI start
- Molecular responders (MR) were defined as patients with a ≥ 50% decrease in TF between tests
- Rw-imaging outcomes, as documented by a provider in their clinical notes, were categorized as complete response (CR), partial response (PR), stable disease (SD), or progressive disease (PD)
- rwOS was defined as time from the imaging date closest to on-treatment xF test to death
- A likelihood ratio test at a two-sided 5% significance level was performed to assess if a Cox proportional hazards model incorporating both xM TRM and rw-imaging as covariates (full model) had predictive power over a model with only rw-imaging as a covariate (reduced model)

SUMMARY

- A dynamic circulating tumor fraction biomarker, xM for Treatment Response Monitoring (TRM), remained a significant predictor of real-world overall survival after accounting for real-world (rw) imaging response (HR=0.3, P=0.02)
- A model with both xM for TRM and rw-imaging predicted rwOS significantly better than a model with rw-imaging alone (Wald's P=0.02)
- Among rw-imaging responders, molecular responders had longer model-predicted rwOS (median=16.0 months) than molecular non-responders (median=9.9 months)

RESULTS

Variable		Value
Cohort size	N	51
Indication	Breast	9 (18%)
	NSCLC	15 (29%)
	SCLC	12 (24%)
	Other	15 (29%)
Age at IO start	Median (Range)	64 (40-81)
Sex	Female	27 (53%)
Race	Asian	2 (4%)
	Black or African American	6 (12%)
	White	24 (47%)
	Other Race	5 (10%)
	Unknown	14 (27%)
Stage	Stage 3	4 (8%)
	Stage 4	47 (92%)
Treatment	ICI monotherapy	16 (31%)
	ICI + chemotherapy	35 (69%)
PD-L1 status	Negative	7 (14%)
	Positive	8 (16%)
	Unknown	36 (71%)
Line of Therapy	1L	29 (57%)
	2L+	22 (43%)

Table 1. Clinical characteristics of patients evaluable with real-world imaging outcomes

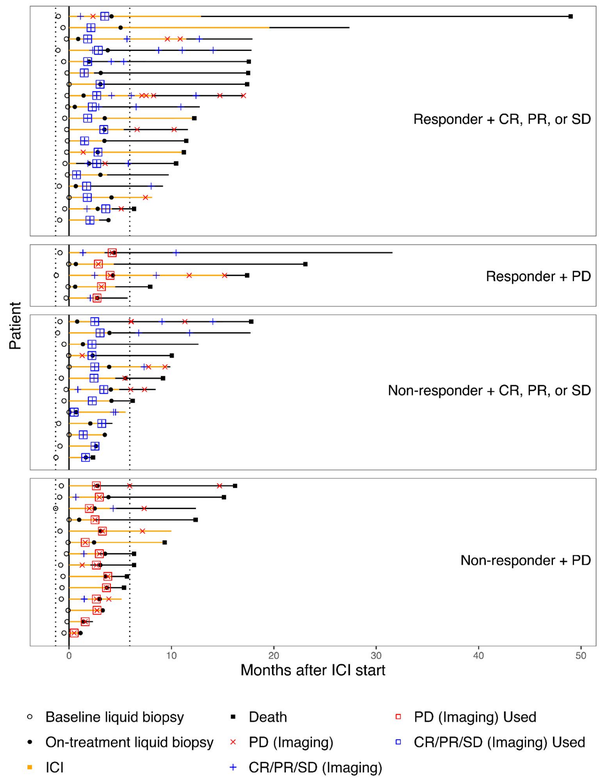

Figure 1. Swimmer plot showing timeline of baseline and on-treatment xF testing and rw-imaging used for making response classifications.

N=51	CR/PR/SD	PD
Molecular Responder	N=19 (59%) Median predicted rwOS: 16.0 months	N=5 (26%) Median predicted rwOS: 15.3 months
Molecular Non-responder	N=13 (41%) Median predicted rwOS: 9.9 months	N=14 (74%) Median predicted rwOS: 7.8 months

Table 2. Risk stratification based on molecular response and real-world response; percentages show molecular response breakdown per real-world response category.

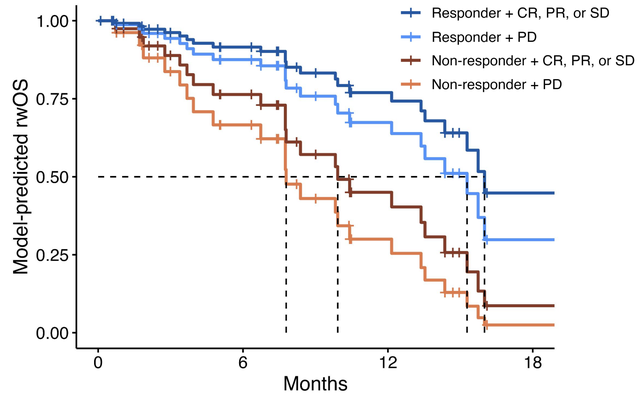

Figure 2. Model-predicted rwOS KM curves based on a model combining molecular and imaging-based response. The full model (MR vs. nMR HR=0.3, CI=0.1-0.8, p=0.02; rw-imaging response vs. rw-imaging non-response HR=0.7, CI=0.3-1.5, p=0.3), shown above, is superior in predicting rwOS (p=0.02) to the reduced model of only rw-imaging response (rw-response vs. rw-non-response HR=0.5, CI=0.2-1.2, p=0.1).

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