34 **ASSOCIATION OF A NOVEL CIRCULATING TUMOR FRACTION DNA BIOMARKER OF TREATMENT RESPONSE MONITORING AND CLINICAL OUTCOMES IN A REAL-WORLD, DIVERSE PAN-CANCER COHORT TREATED WITH IMMUNOTHERAPY**

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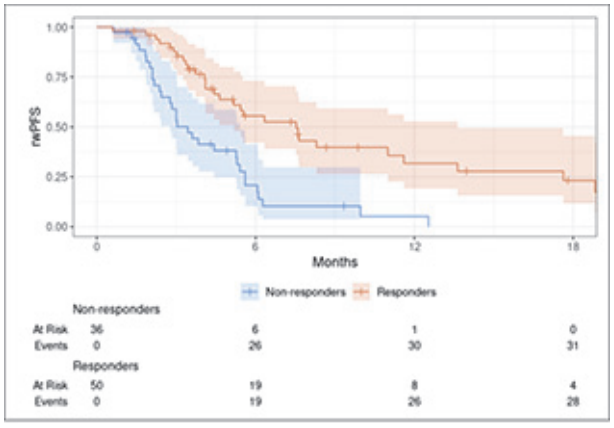
Background Clinical evidence suggests that early changes in circulating tumor DNA fraction estimates (ctFEs) may be predictive of immune checkpoint inhibitor (ICI) response. However, data on the validity and utilization of this biomarker in clinical practice is lacking. Further, existing biomarkers often track mutations from small panels and exclude non-mutational events. We present a novel approach for estimating ctFE (denoted xF Monitor) utilizing diverse genomic events, and the association of changes in ctFEs with ICI outcomes in a real-world pan-cancer cohort.

Methods ctDNA profiling was performed using the Tempus xF liquid biopsy assay of 105 genes. ctFE is computed by applying an ensemble algorithm incorporating copy number variant data, and somatic and germline variant allele frequencies (VAFs). The limit of blank (LOB) was established using 20 presumed-healthy samples. The accuracy of the ctFE algorithm was evaluated using held-out 17 presumed-healthy plasma samples and 124 clinical plasma samples and compared against performance of a median VAF approach.

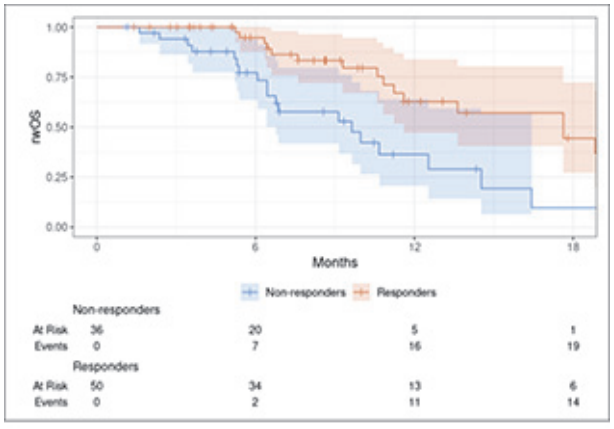
Deidentified patient records from the Tempus multimodal database were analyzed if patients had an xF test ≤ 60 days prior to the start of ICI (alone or in combination with chemotherapy (CT)) and an xF test 15–180 days post-ICI. Patients were evaluable if they had ctDNA > LOB at baseline. Molecular responders (MR) were defined as patients with a >25% decrease in cTFE between tests. Clinical endpoints were defined from ICI start to the first progression event or death (rwPFS) or death (rwOS), both censored on the last follow-up in event-free patients.

Results The evaluable pan-cancer cohort (n= 86 patients, median age 63 yrs, F = 38%) had > 10 solid tumor types (49% with lung diagnosis). The majority of patients received ICI + CT (66%). The baseline ctFE detection rate was 76%, with a median ctFE of 7.3%. The ctFE algorithm showed improved sensitivity and specificity compared to median VAF, 100% vs. 97%, and 100% vs. 80%, respectively. MRs, with a median decrease from baseline of 83%, had significantly longer rwPFS (HR=0.34, p<0.001, figure 1) and rwOS (HR=0.35, p=0.002, figure 2) than non-MRs.

Conclusions xF Monitor is a novel serial quantitative cTFE algorithm off the Tempus xF assay that has the potential to be used clinically as a predictive biomarker to stratify patients who are likely to benefit from ICI therapy, sparing ineffective therapeutic approaches. The xF Monitor biomarker needs to be prospectively validated in a larger cohort.



Abstract 34 Figure 1 Real-world progression-free survival by molecular response.



Abstract 34 Figure 2 Real-world overall survival by molecular response.

http://dx.doi.org/10.1136/jitc-2023-SITC2023.0034