FOUNDATIONONE® TRACKER
POWERED BY natera

Technical Specifications

FoundationOne®Tracker is a clinical test performed exclusively as a laboratory service as a custom-built, personalized assay for oncology that is based on patient-specific somatic variants (PSVs; substitutions and select indels) identified from tumor tissue testing and used to longitudinally track plasma circulating tumor DNA (ctDNA) abundance as a biomarker for tumor burden dynamics.

Methods

- FoundationOne Tracker uses patient-specific variants (PSVs) identified from a separate baseline tumor tissue test derived from FoundationOne CDx at Foundation Medicine on DNA extracted from formalin-fixed, paraffin-embedded (FFPE) tumor tissue sequenced using a next-generation sequencing (NGS) assay that targets >300 cancer-related genes.
- FoundationOne Tracker uses these PSVs to design a custom-built multiplex PCR NGS assay.
- Whole blood samples are collected and cell free DNA (cfDNA) is extracted from isolated plasma
- cfDNA is sequenced and analyzed using the patient-specific assay.
- Results reported include whether circulating tumor DNA (ctDNA) was detected, as demonstrated by the mean tumor molecules per mL of plasma ctDNA (MTM/mL).
- ctDNA detection is defined as ≥2 PSVs detected.

Analytical Validation Summary

FoundationOne Tracker analytical validation included four studies to measure **Sensitivity** and **Specificity** of ctDNA detection and the **Accuracy** and **Precision** of quantification of ctDNA in MTM/mL.[1]

- **Sensitivity** of the assay for calling samples ctDNA positive (defined as ≥2 PSVs detected) was measured at the limit of detection in contrived samples.
- **Specificity** of the assay for calling samples ctDNA negative was assessed by measuring the negative rate in healthy donor samples and subtracting the estimated false positive rate from designing multiplex PCR NGS assays to non-tumor derived variants.
- **Accuracy** of MTM/mL measurement was calculated by comparing the expected mean variant allele frequency (VAF) (a component of MTM/mL measurement) of a sample to the observed mean variant allele frequency in the assay across the reportable range and performing linear regression analysis.
- **Precision** of the MTM/mL measurement was assessed by measuring the co-efficient of variation of mean variant allele frequency in replicate samples across the reportable range of the assay.

CHARACTERISTIC	ANALYSIS	ANALYTICAL PERFORMANCE
Analytical Sensitivity	Percentage of positive ctDNA detected calls at MTM/mL ≥5 and <10	>94.6%†
Analytical Specificity	True negative rate in healthy donor samples minus the false positive rate from tracking of non-tumor derived variants	>96.52%
Analytical Accuracy	Linear regression analysis performed on samples at ≥0.5% mean VAF confirmed by an orthogonal method	Slope estimates: >1.00 and ≤1.044 Intercept estimates: ≥–0.0005 and <0
Analytical Precision	Percent coefficient of variation (CV) of MTM/mL measured across sample replicates at 10-400 MTM/mL	<11.2%††
Reportable Range	N/A	[0.5,80]% Mean VAF [1,11] mL of Plasma [0.25,200] ng/µL cfDNA concentration

† lower bound of 90% CI
†† upper bound of 90% CI

Reporting

- Test results are provided in an interpretive report including all previously submitted plasma samples at timed intervals from a patient.
- Results reported by FoundationOne Tracker include whether ctDNA was detected and the MTM/mL for each plasma sample.

1 Data on file, Foundation Medicine 2022.

FoundationOne®Tracker is a clinical test performed exclusively as a laboratory service. This test has not been cleared or approved by the U.S. Food and Drug Administration (FDA). FoundationOne Tracker is a personalized assay for oncology that is based on patient-specific somatic variants (substitutions and short insertions/deletions) identified from baseline tumor tissue testing and used to detect and longitudinally measure plasma circulating tumor DNA (ctDNA) abundance as a biomarker for tumor burden. Treatment decisions are the responsibility of the treating physician. ctDNA detection sensitivity may be limited if blood collection occurs within two weeks of surgery or while a patient is on therapy. A negative test result does not definitively indicate the absence of cancer. This test is not designed to detect or report germline variation, nor does it infer hereditary cancer risk for a patient. This test is designed to detect ctDNA from the assayed tumor only; new primary tumors will not be detected. This test is expected to have limited sensitivity in some cancer types due to limited ctDNA shed.

FOUNDATION MEDICINE®

www.foundationmedicine.com | Tel 888.988.3639 | Fax 617.418.2290 | US-FTL-2200023 V1.0