With **ctDNA Tumor Fraction**, the Result is **Clear**

FOUNDATION MEDICINE®

More confidence in positive and negative results

Most liquid biopsy tests offer a blurred image. True positive results stand out, but negative results are harder to interpret.

The clinical trial assay based on FoundationOne®Liquid CDx (IUO) can offer a clearer picture with ctDNA tumor fraction to support trial enrollment—even for wild-type biomarkers that rely on a confident negative result.

Ready for **trial enrollment for wild-type criteria**, such as *EGFR*/*ALK*-negative for immunotherapy

ALK AR BRAF BRCA1 BRCA2 EGFR ESR1 FGFR1 FGFR2 FGFR3 KRAS NTRK1 NTRK2 NTRK3 PIK3CA ROS1

Negative Result from a Liquid Biopsy Test **Without** Tumor Fraction Across Solid Tumors

Is the blood sample negative for actionable variants? Without ctDNA tumor fraction, a negative liquid biopsy result is unclear.

Negative Result from a **Foundation Medicine** Liquid Biopsy Test **With ctDNA Tumor Fraction**

Samples with ctDNA tumor fraction ≥1% have greater confidence in a true negative result

ctDNA fumor fraction is the **key driver** of liquid biopsy concordance for **tissue-detected driver alterations**.[1]

RESULTS **WITHOUT** TUMOR FRACTION		RESULTS **WITH** TUMOR FRACTION	
NSCLC (n=1,036)	**CRC** (n=414)	**NSCLC** (n=312)	**CRC** (n=192)
63% negative predictive value (NPV)	**70%** negative predictive value (NPV)	**94%** negative predictive value (NPV)	**98%** negative predictive value (NPV)

In paired tissue samples with a **negative** liquid biopsy result, **no driver mutations were seen** when **ctDNA tumor fraction ≥1%** (0/24)—offering **confidence in a true negative**.[1]

\+ **Driver-positive** liquid biopsy can **guide trial enrollment for therapy**.

\- **Driver-negative** can:

- **Informative negative with ctDNA tumor fraction ≥ 1%.** *Guide trial enrollment for therapy—even for wild-type biomarkers.*
- **Indeterminate negative with low ctDNA tumor fraction.** *Suggests potential for benefit with reflex tissue CGP testing where driver alterations are frequently detected.*

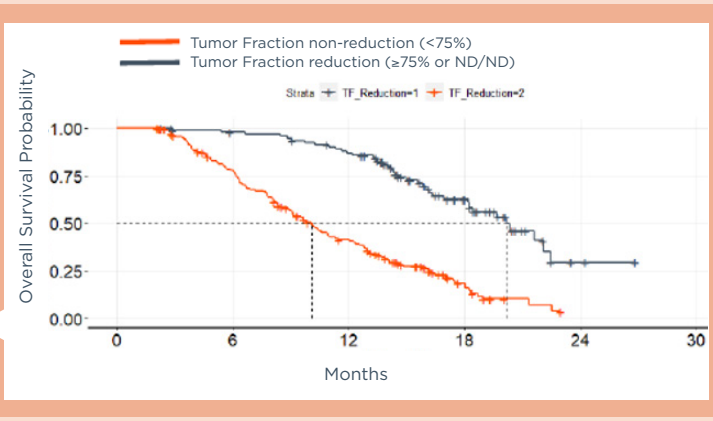
Insights on **molecular response add value** and **complement imaging**.

Standard imaging to assess treatment response can take **months**, and the results can be **inconclusive**. Is a small visual change in tumor volume a signal of response, stability or progression?

FoundationOne®Monitor can add to this signal by showing **changes in ctDNA tumor fraction** to provide insights on molecular response that **complement imaging**.[2]

Changes in ctDNA tumor fraction from **pre-treatment** to an **early on-treatment timepoint** can provide insights into molecular response.[3]

Example: Retrospective analysis of mCRPC subjects showed clear stratification when ctDNA tumor fraction decreased by ≥75% or was not detected from pre-treatment to on-treatment



ctDNA tumor fraction provides a clearer picture compared to variant allele frequency (VAF) by combining a multi-omic assessment of DNA with filtering for clonal hematopoietic (CH) variants, which can confound VAF alone.[4,5]

CH variants can confound ctDNA assessment based on VAF alone, with examples of variants with an increase, decrease or no change in VAF across treatment timepoints—**leading to less clear picture of molecular response**.

ctDNA tumor fraction incorporates **CH filtering** to provide a **more precise estimate of ctDNA than VAF assessment alone**.[6]

FAST ANSWERS

Get insights on ctDNA tumor fraction quickly to add **value to your clinical programs** or **translational research**.

8 days
PROSPECTIVE RESULTS

14 days
RETROSPECTIVE RESULTS

The studies above used the clinical trial assay based on the Foundation Medicine liquid platform. The ctDNA tumor fraction algorithm used in these studies is for research use only.

References

1. Rolfo CD et al. Utility of ctDNA Tumor Fraction to Inform Negative Liquid Biopsy (LBx) Results and Need for Tissue Reflex in Advanced Non-Small Cell Lung Cancer (aNSCLC). J Clin Onc. 2023; 41(16): 9076-9076. DOI: 10.1200/JCO.2023.41.16_suppl.9076.
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3. Sweeney C, Xu C, He J, et al. Evaluation of Circulating Tumor DNA Kinetics as a Prognostic Biomarker for Overall Survival in Metastatic Castrate Resistant Prostate Cancer. Cancer Res 2023; 83(7_Supplement): 3362. DOI:https://doi.org/10.1158/1538-7445.AM2023-3362.
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5. Husain H, Pavlick DC, Fendler BJ, et al. Tumor Fraction Correlates with Detection of Actionable Variants Across >23,000 Circulating Tumor DNA Samples. JCO Precis Oncol. 2022 Oct;6:e2200261. doi: 10.1200/PO.22.00261.
6. Rolfo CD, Madison R, Pasquina LW. Utility of ctDNA Tumor Fraction to Inform Negative Liquid Biopsy (LBx) Results and Need for Tissue Reflex in Advanced Non-Small Cell Lung Cancer (aNSCLC). J Clin Onc. 2023; 41(16): 9076-9076. DOI: 10.1200/JCO.2023.41.16_suppl.9076.

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