LIQUID BIOPSY TO IDENTIFY ACTIONABLE BIOMARKERS IN mNSCLC

Tissue-based testing is the gold standard but is not always available[1]

- **~20%** of patients have inadequate tumor tissue for molecular analysis at diagnosis[2,3]
- Repeat biopsies are not feasible in almost **20%** of patients with advanced NSCLC[3]
- Almost **25%** of repeat biopsies fail to yield sufficient material for genomic analysis[3]

A prospective study of 323 patients with mNSCLC who had blood-based biomarker testing ordered as part of routine clinical management showed that[4]:

44% of eligible patients were unable to get complete genomic results from tissue biopsy

~2× as many patients had targeted alterations detected by liquid biopsy and tissue testing (n=82) vs tissue testing alone (n=47)

Liquid biopsy is a diagnostic technique that measures either cell-free DNA (cfDNA), circulating tumor cells (CTCs), or tumor exosomes from bodily fluids such as blood, urine, or saliva[5,6]

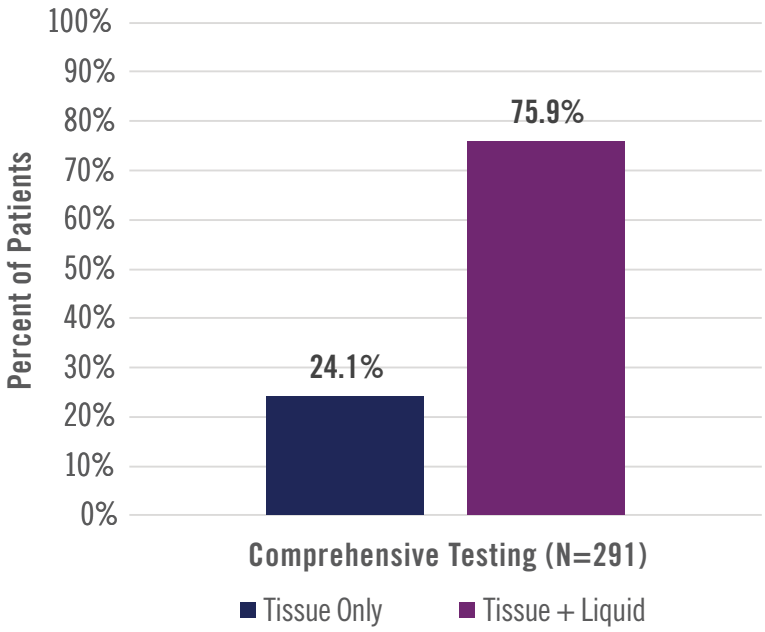
Liquid biopsy may be used to test for important biomarkers in NSCLC including *ALK, BRAF, EGFR, MET, RET, and ROS1*[7-9]

- Multiple liquid biopsy tests are FDA approved as companion diagnostics for specific mutations[8,9]

Liquid biopsies can help ensure patients receive comprehensive biomarker testing[10]

A retrospective cohort study of 330 patients with non-squamous stage IV NSCLC assessed the impact of paired tissue and plasma-based NGS on the comprehensiveness of genetic testing and overall survival (OS)[10]

- Genomic testing was either comprehensive (including *EGFR, ALK, BRAF, ROS1, MET, RET,* and *NTRK*), incomplete (2-6 genes), or not done
- Concurrent tissue and plasma testing significantly increased the proportion of patients undergoing comprehensive testing
- Median OS was 22.1 months in patients who received comprehensive testing and 11.6 months in the incomplete/no testing group
- The data suggest that treatment with a matched therapeutic approach may impact long-term outcomes



- Similar results were seen in the incomplete/no testing group

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Liquid biopsy results demonstrate clinical applicability in the NSCLC treatment paradigm[11,12]

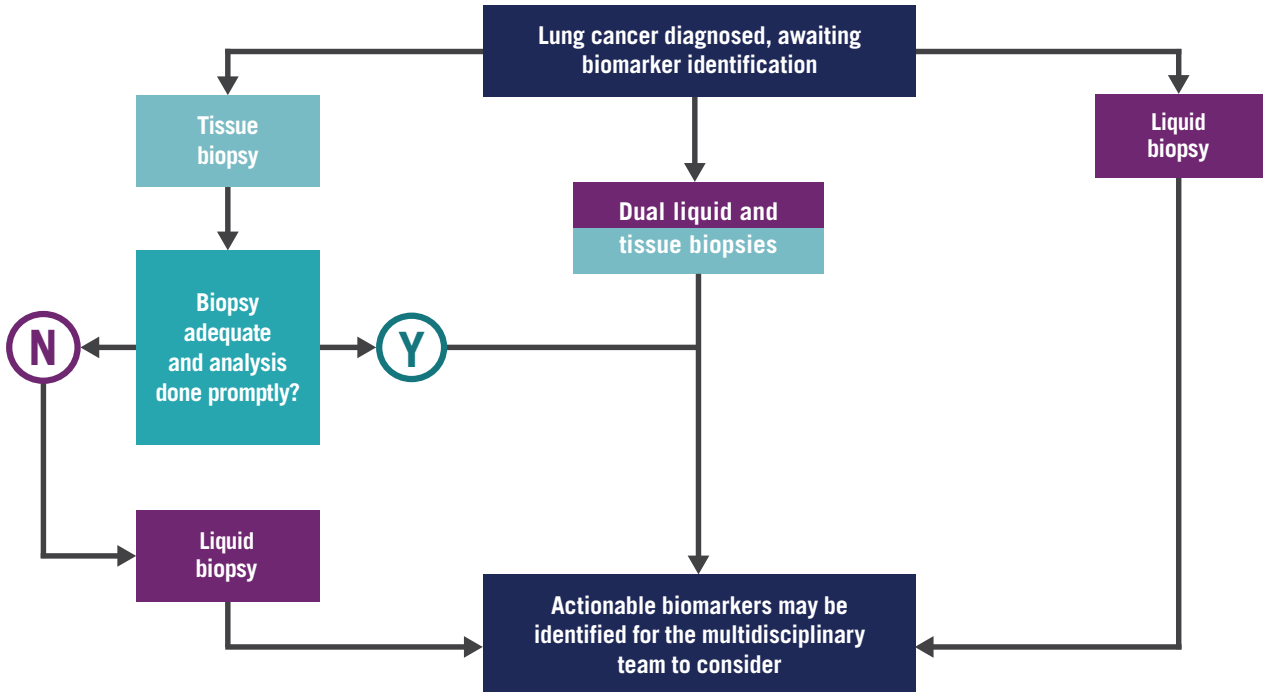
The Blood First Assay Screening Trial (BFAST) is an open-label, multicohort trial that examined outcomes in patients with advanced or mNSCLC whose treatment decisions were driven by blood-based NGS[11,12]

- Of the six BFAST cohorts that have been initiated (*ALK, ROS1, RET, BRAF, EGFR* and *bTMB*), two (*ALK* and *ROS1*) have been completed[11,12]
- So far, the use of blood-based NGS to identify patients with *ALK*+ and *ROS1*+ NSCLC prior to commencement of targeted therapy has demonstrated the **clinical applicability of liquid biopsy–driven diagnostics as a method to prospectively screen patients for actionable mutations**[11,12]

Blood-based NGS has the potential to overcome some of the limitations associated with tissue collection and testing, which may enable clinicians to offer personalized therapies[13]

	NGS on Liquid Biopsy[7-9,13]	NGS on Tissue Biopsy[13,14]
Invasiveness	Peripheral blood draw	Invasive surgical procedure
Turnaround time	Rapid	Slower
Evidence for treatment selection	Emerging	Established
Sample requirement (per lab guidance)	10-20 mL blood	>8 slides

Potential ways to incorporate liquid biopsies in practice[15]



mNSCLC = metastatic NSCLC; NGS = next-generation sequencing; NSCLC = non-small cell lung cancer.

References: **1**. Bonanno L, et al. *Br J Cancer.* 2022;127:383–393. **2.** Lim C, et al. *Ann Oncol.* 2015;26:1415-1421. **3.** Chouaid C, et al. *Lung Cancer.* 2014;86:170-173. **4.** Aggarwal C, et al. *JAMA Oncol.* 2019;5:173-180. **5.** Gold B, et al. *J Mol Diagn.* 2015;17:209-224. **6.** Diaz LA, et al. *J Clin Oncol.* 2014;32:579-586. **7.** FoundationOne Medicine. https://www.foundationmedicine.com/test/foundationone-liquid. August 29, 2022. **8.** Guardant Health. https://guardanthealth.com/. Accessed August 29, 2022. **9.** NeoGenomics. https://neogenomics.com/diagnostic-services/specialty-testing/liquid-biopsy. Accessed August 29, 2022. **10.** Aggarwal C et al. *J Clin Oncol.* 2022;40:16_suppl, 9022-9022. **11.** Dziadziuszko R, et al. *Transl. Oncol.* 2021;16:2040-2050. **12**. Peters S, et al. *J. Clin Oncol.* 2022;40(17):1. **13.** Merker JD, et al. *J Clin Oncol.* 2018;36:1631-1641. **14.** Hovelson DH, et al. *Neoplasia.* 2015;17:385-399. **15.** Rolfo et al. *J Thorac Oncol.* 2021;16(10):1647-1662.

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