Concordance Between Solid Tissue and Liquid Biopsy for Gene Mutations in Advanced Cancer Patients: Single Center Study

Authors: K Patel, N Olson, R Nadkarni, D Naidu, S Niar, A Patel, C Bogan, S Ramaswamy, E Gillespie, M Sullivan, A Kodali, N Clinton, R Lozano, N Anandpura, H Taylor, S Naidu, N Nathwani, A Gor, V Rabara

Institutions: Carolina Blood and Cancer Care Associates, No One Left Alone, Community Clinical Oncology Research Network

Abstract

Background: Liquid biopsy is a promising alternative to tissue biopsy for detecting actionable mutations in cancer, but concordance between the two remains under investigation.

Methods: We retrospectively analyzed 501 advanced cancer patients (stage III/IV) who underwent next-generation sequencing (NGS) in 2022. Of these, 106 had both solid tumor and plasma-derived ctDNA testing.

Results: Among the 106 patients, 46.2% showed concordant actionable mutations across both tests. Most patients (87%) had stage IV disease; 76% were newly diagnosed. Frequent concordant mutations included TP53, PTEN, KRAS, ERBB2, PIK3CA, and BRAF.

Conclusions: Liquid biopsy offers faster and less invasive testing but lacks full concordance with tissue NGS. A sequential testing strategy—beginning with liquid biopsy and confirming negative results via tissue NGS—may optimize clinical utility. Further large-scale studies are needed to confirm assay sensitivity and specificity.

Keywords: Liquid biopsy, ctDNA, NGS, mutation detection, cancer diagnostics, precision oncology

Introduction

Precision oncology depends on accurately identifying genomic alterations, traditionally through solid tumor biopsies. However, these are invasive and limited by tumor heterogeneity and accessibility issues. Liquid biopsies have emerged as a noninvasive alternative, capable of detecting tumor-derived materials (e.g., ctDNA, CTCs, exosomes) across various cancer stages. They offer advantages for diagnosis, prognosis, treatment guidance, and disease monitoring. While advances have improved the sensitivity of liquid biopsy (detecting ctDNA at very low levels), questions remain about how well results from liquid biopsies align with those from solid tumor next-generation sequencing (NGS), especially in real-world settings. The study referenced aims to evaluate this concordance in a diverse patient population with advanced cancer, helping clarify the clinical value of liquid biopsy in everyday oncology practice.

Materials and Methods

Study Design:

A retrospective observational study was conducted at a community cancer center, including all stage III/IV cancer patients who underwent NGS testing in 2022. Liquid biopsy was offered when tissue samples were unavailable or insufficient, pending insurance approval.

Testing Procedures:

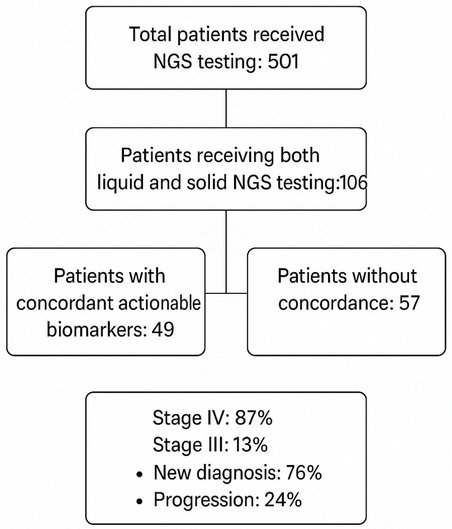
- Solid tumor NGS: Performed on FFPE tissue from primary or metastatic sites.
- Liquid biopsy: Conducted on plasma-derived ctDNA from 10–20 mL of blood in DNA preservation tubes.
- Both methods used commercially available NGS panels targeting cancer-related genes to detect SNVs, indels, CNAs, and select gene fusions.

Data Collection & Analysis:

Data included demographics, cancer type, stage, treatment status, time to testing, and result turnaround time.

- Primary outcome: Concordance of actionable mutations between the two methods (identical alterations).
- Secondary analysis: Frequencies and types of concordant mutations.
- Descriptive statistics and concordance rates were calculated using standard software.

Figure 1: Patient Selection Flow Diagram



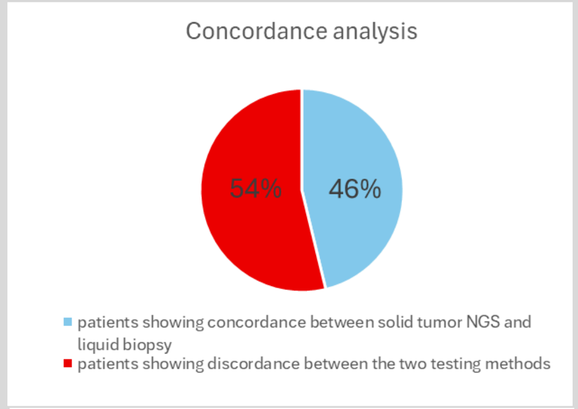


Figure 2: Concordance Analysis Pie Chart
The pie chart depicts the breakdown of concordance analysis results:
Blue segment (46.2%): Patients showing concordance between solid tumor NGS and liquid biopsy (n=49)
Red segment (53.8%): Patients showing discordance between the two testing methods (n=57)

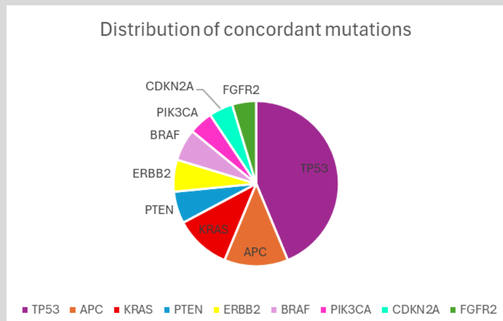


Figure 3: Distribution of Concordant Mutations Pie Chart
This colorful pie chart illustrates the distribution of the most commonly discovered mutations with concordance between both testing methods:
TP53 (purple, largest segment): 28 patients
APC (orange): 8 patients
KRAS (red): 7 patients
PTEN (blue): 4 patients
ERBB2 (yellow): 4 patients
BRAF (light purple): 4 patients
PIK3CA (pink): 3 patients
CDKN2A (teal): 3 patients
FGFR2 (green): 3 patients

Mutation	Frequency	Mutation	Frequency
TP53	28	ERBB2	4
PIK3CA	3	TMB	1
APC	8	H3F3A	2
ARID1A	1	NF2	1
KRAS	7	MDM2	2
BRAF	4	MLH1H	1
ERBB2	4	EGFR	1
PIK3R1	1	CDK4	1
CDKN2A	3	FGFR1	3
CHEK2	1	CCND1	1
PIK3CA	2	ERBB3	1
ATM	2	BAP1	1
NF1	1	BRCA2	2
RB1	1	KRAS	1
AKT1	1		

Figure 4: Comprehensive Mutation Frequency Table The table presents all identified actionable mutations with concordance between liquid biopsy and solid tumor NGS:

Discussion

Advantages of Liquid Biopsy:

Noninvasive and Accessible: A simple blood draw enables testing, avoiding the risks of invasive tissue biopsies and making it suitable for routine and serial monitoring.

Addresses Tumor Heterogeneity: Captures DNA from both primary and metastatic sites, giving a more complete genomic picture.

Technological Advances: Tools like digital droplet PCR and deep sequencing have improved mutation detection, including in therapy selection and early recurrence monitoring.

Limitations and Challenges:

Sensitivity Issues: Low levels of ctDNA in early-stage cancers can lead to false negatives.

Influencing Factors: Tumor size, location, and biology impact ctDNA shedding and detectability.

Cost and Expertise: High costs, inconsistent insurance coverage, and need for specialized interpretation limit widespread use.

Lack of Large Prospective Data: More robust clinical trials are needed to validate and standardize its use.

Concordance Analysis:

Study Findings: 46.2% concordance between liquid biopsy and tissue NGS, in line with prior studies.

Most Concordant Mutations: TP53 mutations showed the highest concordance due to their early and frequent occurrence in cancers.

Reasons for Discordance: Tumor heterogeneity, treatment-driven mutation evolution, and technical assay differences.

Clinical Implications & Future Directions:

Sequential Testing Approach: Start with liquid biopsy; if negative or incomplete, follow up with tissue biopsy—balancing cost, invasiveness, and accuracy.

Future Focus: Standardize testing protocols and conduct large prospective studies to confirm clinical utility and improve adoption in personalized oncology.

Conclusion

Liquid biopsies offer a promising, less invasive method for detecting actionable mutations in advanced cancer patients, especially when tissue samples are inadequate. However, their limited concordance with solid tumor next-generation sequencing (NGS)—only 46.2% in this study—raises concerns about using them as the sole diagnostic tool.

A safer, more effective strategy may involve:

- Starting with liquid biopsy for speed and ease
- Following up with tissue-based NGS if the liquid biopsy is negative or inconclusive

This sequential or combined approach may improve accuracy, cost-effectiveness, and clinical utility.

Recommendations for Future Research:

- Enhance sensitivity and reliability of liquid biopsy assays
- Standardize protocols across institutions
- Conduct large, prospective clinical trials to confirm utility in different cancer types and settings

This balanced diagnostic strategy could ensure faster and more accurate treatment decisions in advanced cancer care.

References

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