INTRODUCTION
The extensive clinical research conducted to date clearly showed that liquid biopsy can provide information on the molecular status of cancer at any disease stage of the tumor, whether primary or metastasis stage (Wang et al., 2019), and in a comprehensive way which could strongly help oncologists in treatment guidance, particularly in identifying abnormalities leading to cancer initiation, to make treatment decisions and to monitor patient response to treatment.3,4

Liquid biopsy, with its potential for diagnostic, prognostic, monitoring, and therapeutic applications, is an emerging field in cancer management, offering noninvasive testing options. This approach primarily targets tumor traces like CTC, circulating tumor exosomes, ctDNAs, and circulating tumor RNAs. However, its optimal application is constrained by the lack of large-scale prospective studies comparing mutation detectability between solid tumor NGS analysis and liquid biopsy. In our study, we assess the concordance between liquid biopsy and solid tumor NGS in our patient population to address this gap.

This study explores the potential of liquid biopsies, using plasma-based NGS assays, for identifying actionable biomarkers in advanced-stage cancer patients. While traditional solid tumor biopsies may be challenging and limited by intratumor heterogeneity, liquid biopsies offer promise in detecting relevant mutations. The study examines the concordance between ctDNA detection in liquid biopsies and solid tumor NGS in a diverse community cancer clinic with advanced-stage patients. This research aims to address the application of liquid biopsies in patient management and their potential in improving personalized cancer treatment.

RESULTS
We carried out NGS testing in 501 patients at our cancer center in 2022. Of these patients 106 patients received both solid tumor NGS testing and plasma-derived ctDNA testing using liquid biopsy (Figure 1). 49 if these patients demonstrated concordance between solid tumors and liquid biopsies for various actionable mutations (Figure 2).

We compared the accuracy of a plasma-based NGS assay to solid-tumor-based NGS for several specific actionable targets who had received concurrent testing with both a solid-tissue-based NGS assay and a commercially available plasma-based NGS assay. Patients represented both new diagnoses (76%) and disease progression on treatment (24%); the majority (87%) had stage IV disease.

Most discovered mutations in concordance were P53, PTEN, KRAS, ERBB2, PIK3CA, BRAF, APC, CDKN2A, FGFR2 (Figure 3).

DISCUSSION
• The key advantage of liquid biopsy is its ability to overcome the limitations of tissue biopsies, such as limited tissue availability, challenges related to tumor heterogeneity, and difficulties in reaching certain tumors.
• Liquid biopsy can identify important molecular markers and offer an aggregate of ctDNA from both primary and metastatic sites, addressing tumor heterogeneity.
• The convenience of liquid biopsy is underscored by its ability to be performed with a simple blood draw, making it accessible in various clinical settings, including mobile phlebotomy.

Limitations and Challenges
• It may be challenging to detect tiny DNA variations in the blood, particularly in cases with a small volume of cancer.
• False negatives can occur due to low ctDNA levels, necessitating tissue biopsies in some instances.
• The cost of ctDNA testing is often high, and insurance coverage varies.
• Large-scale prospective data is still lacking, hindering the universal adoption of liquid biopsy as a standard test.

CONCLUSION
While liquid biopsies present as a new technology that may allow for management of advanced cancer patients reducing time to testing, circumventing insufficient quantity of tissue or poor-quality specimen for suitability, lack of full concordance of all actionable mutations place a challenge at initial assessment. Safer approach may be that liquid biopsy may be ordered initially with default to solid tumor NGS where early detection of actionable mutation may offer rapid intervention and in the event of negative result, tissue based NGS testing may complete the circle if need be. This approach may be cost effective and full of clinical utility and validity. Large scale studies may demonstrate that these assays have both the sensitivity and specificity required to correctly identify appropriate actionable mutations. In the interim identifying actionable mutations may be a safer approach in individual patients.

REFERENCES