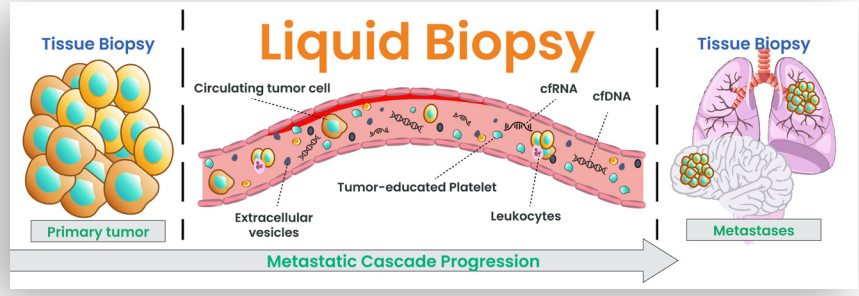
Case Study
ESR1

Detected by GTC's Liquid Trace™ Solid Tumor

Monitoring Clonal Evolution
in Breast Cancer Using Liquid Trace

GENOMIC® TESTING COOPERATIVE



Discussion

Endocrine therapy is the main treatment option for Estrogen receptor-positive (ER+) breast cancer (BC). Compared with other clinical subtypes, ER+ BC patients usually have a more favorable prognosis. However, almost all ER+ BC patients develop endocrine resistance and disease progression eventually. Mutations in Estrogen Receptor 1 (ESR1) play a key role in resistance to Aromatase Inhibitors but may retain sensitivity to selective estrogen receptor degraders (SERD). Recently, Elacestrant, an oral SERD, was approved for patients with ER+/HER2- ESR1 mutant metastatic breast cancer. Detection of PIK3CA mutations is important as well, since recently Alpelisib in combination with Fulvestrant with HR+/HER2- PIK3CA mutant metastatic breast cancer. Detection of ESR1 and PIK3CA could also have important clinical applications for the follow-up of these patients. In this case the patient breast cancer tissue was sequenced initially and treated accordingly. ESR1 mutation was not detected in the diagnostic tissue sample. Later on, the patient's disease progressed and relapsed. A minimally invasive liquid biopsy was performed and ESR1 mutation was detected indicating endocrine resistance.

In summary, novel selective estrogen receptor degraders (SERDS) and PIK3CA inhibitors are emerging as new therapeutic options in metastatic breast cancer. The analysis of cfDNA and cfRNA allows for non-invasive monitoring of these mutations over time, providing clinicians with valuable information about treatment response, disease progression, and the emergence of resistance. This approach reduces the need for invasive tissue biopsies and enables real-time monitoring of the tumor's genetic profile, facilitating personalized treatment decisions. Furthermore, Trace liquid biopsy can be used as tissue informed test for monitoring response and minimal residual disease with high sensitivity but at the same time detecting clonal evolution of the development of new mutations.

References

1. Combining cell-free RNA (cfRNA) with cell-free total nucleic acid (cfTNA) as a new paradigm for liquid biopsy. Maher Albitar, Hong Zhang, Ahmad Charifa, Andrew Ip, Ivan De Dios, Wanlong Ma, James K. McCloskey, Michele Donato, David Samuel DiCapua Siegel, Stanley E. Waintraub, Martin Gutierrez, Andrew L Pecora, Andre Goy. DOI: 10.1200/JCO.2022.40.16_suppl.3048 Journal of Clinical Oncology 40, no. 16_suppl (June 01, 2022) 3048-3048.
2. Detection of ESR1 Mutations Based on Liquid Biopsy in Estrogen Receptor-Positive Metastatic Breast Cancer: Clinical Impacts and Prospects. Liao H, Huang W, Pei W, Li H. Front Oncol. 2020 Dec 15;10:587671. doi: 10.3389/fonc.2020.587671.

Background

Circulating tumor DNA and RNA (cfDNA, cfRNA) is cell-free DNA/RNA released by tumor cells in the blood. cfDNA and cfRNA can be detected in the plasma of patients with cancer, and their analysis represents a minimally invasive tool for detecting and monitoring key gene mutations and alterations. In breast cancer, detection of ESR1 and PIK3CA mutations is very important, since recently there have been specific targeted therapies developed.

Clinical History

- 62-year-old female
- With relapsing (ER+/HER2 -) breast cancer

Molecular Profiling Findings

- Mutations in ESR1, PIK3CA, MAP3K1, PRKDC, KMT2C, MYC, ROS1, NOTCH2, and EP300 genes

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