

# Monitoring *ESR1* Mutations in Metastatic Breast Cancer

Patients with advanced receptor positive breast cancer are typically treated with aromatase inhibitors along with cyclin-dependent kinase 4/6 inhibitors. Together these drugs reduce estrogen levels in the body and block cancer cell growth. Overtime, the cancer cells adapt and develop mutations that cause this drug combination to no longer be effective. One of the more common resistance causing mutations are found in the estrogen receptor (*ESR1*) itself, resulting in estrogen-independent growth of the breast cancer cells. Recent clinical trials (described below) have demonstrated the clinical value of monitoring for these *ESR1* mutations (*ESR1m*), including modifying the drug regimen to maintain the therapeutic response. As a result, monitoring for *ESR1* mutations in advanced receptor positive breast cancer patients is becoming more commonplace in the oncological care of breast cancer.

## PADA-1 Trial

PADA-1, a randomized, open-label, multicenter, phase III trial to evaluate the safety and efficacy of palbociclib in combination with hormone therapy (HT) driven by ctDNA *ESR1* mutation monitoring in ER+, HER2-negative mBC patients.

- The PADA-1 trial aimed to show the efficacy of an early change in therapy at the onset of *ESR1* mutation in blood (b*ESR1*<sup>mut</sup>), while assessing the global safety of combination fulvestrant and palbociclib.

## Results

- Switching therapy to fulvestrant and palbociclib, in patients with detectable *ESR1* mutations, resulted in a doubling of median progression-free survival, from 5.7 months to 11.9 months.
- PADA-1 is the first prospective randomized trial showing that the early therapeutic targeting of b*ESR1*<sup>mut</sup> results in significant clinical benefit.



### PADA-1 Trial

Scan the QR Code or Visit:  
[www.thelancet.com/article/S1470-2045\(22\)00555-1/fulltext](http://www.thelancet.com/article/S1470-2045(22)00555-1/fulltext)

## SERENA-6 Trial

SERENA-6 is a phase III switching trial of camizestrant in *ESR1m* breast cancer during first-line treatment.

- The phase III SERENA-6 trial uses blood tests to monitor if patients with breast cancer develop *ESR1m* while being treated with an aromatase inhibitor and a CDK4/6 inhibitor. An *ESR1m* test will be considered positive if one or more *ESR1* mutations that occur in HR+ mBC are detected. If *ESR1m* is detected, participants will be randomly assigned to either continue with the same aromatase inhibitor or switch to camizestrant while continuing with the same CDK4/6 inhibitor.
- The study will assess whether switching to camizestrant prolongs the time before the cancer grows, spreads, or worsens.

- Camizestrant is an investigational drug that blocks estrogen receptors, including mutated receptors, reducing the growth and spread of cancer. It is a next-generation oral selective estrogen receptor degrader (SERD) that in a phase II study **significantly improved progression-free survival (PFS) over fulvestrant**.
- The aim is to treat *ESR1m* clones and extend the duration of control of ER-driven tumor growth, delaying the need for chemotherapy.

### Background

- Data presented at SABCS in 2022 showed patients with detectable *ESR1* mutations who switched therapies had a near doubling of progression-free survival.
- *Note: Camizestrant has been shown to be more broadly effective against acquired ESR1 mutations than fulvestrant in clinical studies.*



### SERENA-6 Trial

Scan the QR Code or Visit:  
[www.tandfonline.com/doi/full/10.2217/fo-2022-1196](http://www.tandfonline.com/doi/full/10.2217/fo-2022-1196)

Revolutionize *ESR1* Mutation Testing with the QuantideX® qPCR *ESR1* exoMutation Kit\*\* + Exolution™ Plus cfDNA + exoRNA Isolation Kit\*\*



Scan the QR Code or Visit:  
[asuragen.com/portfolio/oncology/quantidex-esr1-exomutation-kit/](http://asuragen.com/portfolio/oncology/quantidex-esr1-exomutation-kit/)

\*This product is under development; performance characteristics and final product features to be determined.

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