Transcript Details

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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

Earlier *ESR1*m Detection May Delay Endocrine Resistance in HR+/HER2- Advanced Breast Cancer

Announcer:
You're listening to ReachMD. This medical industry feature, titled "Earlier *ESR1m* Detection May Delay Endocrine Resistance in HR+/HER2- Advanced Breast Cancer" is sponsored by AstraZeneca.

Narrator:
Two Phase 3 trials in HR-positive breast cancer were designed to explore whether changing from *ESR1* testing at clinical progression to *ESR1* monitoring during first-line treatment may delay endocrine resistance in the advanced or metastatic setting.

To provide context for this monitoring approach, it is important to understand the role of *ESR1* mutations in breast cancer progression. The *ESR1* gene encodes the estrogen receptor protein, which normally becomes activated when it binds to estrogen. But extended exposure to aromatase inhibitors may lead to the development of *ESR1* mutations.

ESR1 activating mutations cause the estrogen receptor-mediated pathway to always be active, even in the absence of estrogen. As the exposure to aromatase inhibitors increases, so does the rate of developing an *ESR1* mutation. Current data suggest that the rate of *ESR1* mutations at diagnosis of advanced breast cancer is about 5%, which may increase up to 40% after progression on an AI regimen in the first-line metastatic setting.

Because endocrine resistance inevitably develops, there is a need to identify alternative approaches to help prolong a patient's time on endocrine therapy. In HR-positive, HER2-negative metastatic breast cancer, the strategy of testing for *ESR1* mutations at progression on first-line treatment is meant to determine eligibility for second-line therapies, including targetable mutations. However, another testing strategy is to monitor circulating tumor DNA for the emergence of *ESR1* mutations during first-line treatment. This may allow for earlier identification of patients at risk of disease progression on their first-line treatment regimen.

Here's how it works. Patients on a first-line regimen typically have routine blood tests. The tumors of those taking an AI regimen are particularly susceptible to developing *ESR1* mutations. Two studies were conducted to determine if integrating early monitoring for *ESR1* mutations into routine blood tests might allow for detecting emerging resistance mutations before disease progression.

If *ESR1* mutations are detected earlier, this monitoring strategy may help identify patients who require alternative treatment approaches, with the possibility of addressing emerging endocrine resistance mechanisms earlier in the patient journey and ahead of disease progression. We'll end with a quick reflection - your perspective matters!

Announcer:
This program was sponsored by AstraZeneca. If you missed any part of this discussion, visit Industry Features on ReachMD.com, where you can be part of the knowledge.

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