Transcript Details

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Rethinking *ESR1* Testing in HR+/HER2− Advanced Breast Cancer

Announcer:
You're listening to ReachMD. This medical industry feature, titled "A Potential Paradigm Shift in Testing Strategies in First-Line HR-Positive, HER2-Negative Advanced Breast Cancer: Can We Identify Emerging Endocrine Resistance Earlier?" is sponsored by AstraZeneca.

Narrator:
Two recent Phase 3 trials in HR-positive breast cancer have been designed to explore whether changing from the current *ESR1* testing strategy to an investigational strategy may delay endocrine resistance in the first-line advanced or metastatic setting.

To provide context for this investigational 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 the *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 suggests 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. The current *ESR1* testing strategy in HR-positive, HER2-negative metastatic breast cancer is to test at progression on first-line treatment to determine eligibility for second-line therapies, including targetable mutations. However, an investigational 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 current treatment regimen.

Here's how it might work. Patients on a first-line regimen typically have routine blood tests every 1 to 3 months. 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 investigational testing strategy may help identify patients who may require alternative treatment approaches, with the possibility of addressing emerging endocrine resistance mechanisms earlier in the patient journey, and ahead of disease progression.

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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