

Novel Treatment Combination Improves Progression-Free Survival in Metastatic Breast Cancer

Experimental hormone therapy giredestrant delayed disease progression in patients with advanced estrogen-receptor-positive/HER2-negative breast cancer.

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Patients with estrogen-receptor-positive HER-2-negative advanced breast cancer showed significantly improved progression-free survival when treated with an oral combination regimen that includes giredestrant, a novel, next-generation selective estrogen receptor degrader and full antagonist, compared to a standard combination approach.

These findings, from the Phase 3 evERA Breast Cancer study, [were presented October 18] by [Dr. Erica Mayer](#) of Dana-Farber Cancer Institute at the annual meeting of the [European Society for Medical Oncology \(ESMO\)](#) in Berlin, Germany.

Tumors that express the estrogen receptor (ER) account for roughly 70% of all breast cancer cases, and metastatic forms of these ER-positive cancers can be difficult to treat. In addition, the development of resistance to current endocrine therapies poses a major challenge for both clinicians and patients, underscoring the need for novel therapies that effectively target this breast cancer subtype.

“There is a significant need for therapies for metastatic ER-positive breast cancers that are more effective, particularly for patients whose tumors develop resistance to current endocrine therapies and who have progressed following treatment with CDK 4/6 inhibitors,” says Dr. Mayer. “In addition, we also need tolerable therapies that partner well with existing targeted agents and overall will improve outcomes for patients in the second line setting and beyond — when resistance is common and can be challenging to overcome.”

Giredestrant is a next-generation selective estrogen receptor degrader and full antagonist or SERD. It works by binding to the estrogen receptor and promoting its degradation, thus preventing estrogen from stimulating cancer growth. This new SERD has two important features compared to existing drugs. First, it has a unique mechanism of action relative to other hormone-blocking agents, which means it could benefit patients who develop resistance to current therapies. Second, giredestrant is administered orally, which is more convenient for patients than the

monthly injections required for first-generation drugs.

evERA is a global Phase 3, randomized, open-label study evaluating the use of giredestrant, in combination with everolimus, an mTOR targeting drug, in patients with ER-positive, HER-2-negative advanced breast cancer. This all-oral regimen is compared to a standard of care combination of endocrine therapy plus everolimus. evERA is the first positive, head-to-head phase 3 study of an all-oral SERD-containing regimen versus a standard of care combination.

A total of 373 patients were enrolled and randomized to receive either giredestrant plus everolimus or standard of care endocrine therapy and everolimus. About 55% of patients had mutations in the estrogen receptor gene (ESR1), indicating potential resistance to endocrine therapy. The study was designed to look for improvement in progression-free survival (PFS) using the giredestrant-based regimen in all patients (intention to treat, ITT) and in the subset of patients whose tumor had the ESR1 mutations.

With a median follow-up of 18.6 months, patients with tumors harboring an ESR1 mutation who received the giredestrant-containing regimen showed a statistically significant improvement in median PFS of 9.99 months, compared to 5.45 months for those who received the standard of care combination. That corresponds to a 63% reduction in the risk of disease progression or death.

In the ITT population, which includes patients with ESR1 mutations and those without, the patients who received the giredestrant combination showed a statistically significant improvement in median PFS of 8.77 months compared to 5.49 months for those treated with the standard of care combination. That corresponds to a 44% reduction in the risk of disease progression or death.

The overall survival data from the study remain immature but are trending favorably. In addition, the safety profile of the giredestrant regimen was manageable and consistent with the known safety profiles of the individual study treatments.

“Although we’ve made great progress in treating metastatic ER-positive, HER-2-negative breast cancer, these cancers can become resistant to existing therapies making them difficult to treat,” says Dr. Mayer. “The combination of giredestrant and everolimus is designed to address the most common resistance mechanisms. The evERA study is the first trial in this setting to show that using this new combination can substantially improve disease control compared to a standard of care combination regimen and may provide great benefit to a large number of patients with advanced breast cancer.”

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