Novel Endocrine Therapy Reduces the Risk of Breast Cancer Recurrence

Giredestrant, a next-generation oral SERD, outperforms long-standing standard therapies for early-stage HR-positive/HER2-negative breast cancer.

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In an international study led by UCLA, researchers have shown that giredestrant, a next-generation oral selective estrogen receptor antagonist and degrader (SERD), when given as an adjuvant therapy for early-stage (I-III) hormone receptor (HR)-positive, HER2-negative breast cancer, significantly lowered the risk of the disease returning when compared with standard hormone therapies long considered the backbone of treatment.

The finding points to a potential new treatment option for the most common subtype of breast cancer, which accounts for roughly 70% of all cases and is most often diagnosed at Stage I, II or III.

The results were shared today [December 10] at the San Antonio Breast Cancer Symposium (SABCS) by global principal investigator, Dr. Aditya Bardia, professor of medicine at the David Geffen School of Medicine at UCLA and director of Translational Research Integration at the UCLA Health Jonsson Comprehensive Cancer Center.

“This is a very significant development, and considering the scope, perhaps one of the most important breast cancer advances in recent years for hormone receptor-positive disease,” said Bardia. “For decades, tamoxifen and aromatase inhibitors have been the standard endocrine therapies, and these findings show a clear improvement with giredestrant. It has the potential to reshape clinical practice for a large proportion of patients with breast cancer.”

Many patients with this type of breast cancer are treated with surgery followed by endocrine therapy, like tamoxifen and aromatase inhibitors, for at least five years after surgery to lower the risk of recurrence. While overall survival rates are high, up to a third of patients see their cancer return and struggle to tolerate current treatments that can make the long treatment course difficult to maintain.

Giredestrant is part of a newer class of medicines built to block and dismantle estrogen receptor signaling, a key driver of growth in HR-positive tumors. Unlike older therapies, it’s engineered to more precisely shut down the pathways that help cancer cells persist.

To test whether this new therapy could meaningfully improve outcomes for patients, researchers enrolled 4,170 people with HR-positive, HER2-negative breast cancer into the phase III lidERA clinical trial. Participants were randomly assigned to receive either 30 milligrams of giredestrant (2,084) or one of several standard endocrine therapies (2,086) for up to five years. The median age of participants was 54 and 59% were postmenopausal.

After a median follow-up of 32.3 months, researchers found patients treated with giredestrant were 30% less likely to have invasive disease recur or progress. The study's secondary endpoint, distant disease-free survival — meaning the time until cancer spreads to other organs — also favored giredestrant, with a 31% reduction in distant metastases.

Common side effects, including joint aches, hot flashes and headaches, occurred at similar rates in both groups and were primarily low-grade. Fewer patients receiving giredestrant discontinued treatment due to side effects (5.3% vs. 8.2%). Mild, asymptomatic bradycardia occurred more frequently with giredestrant, but rarely required intervention.

Longer follow-up is still needed, but if confirmed, Bardia said the findings could mark the first major change in adjuvant endocrine therapy for breast cancer in more than 25 years.

"This represents an exciting advance for patients and the field," Bardia said. "As clinicians, our goal is always to prevent recurrence and help patients live longer, healthier lives and these results bring us closer to that."

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