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Duke Researchers Play Key Role in New Breast Cancer Drug

Elacestrant is first endocrine therapy approved for breast cancer since 2002

ONCOLOGY

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Published March 7, 2023

Research that originated in a Duke Cancer Institute (DCI) laboratory contributed to recent FDA approval of the first new endocrine therapy for breast cancer since 2002, and the only drug designed to target mutations in estrogen receptor 1 (ESR1).

Donald P. McDonnell, PhD, associate director for translational research at DCI and the Glaxo-Wellcome Distinguished Professor of Molecular Cancer Biology, directed the research team that led to the development of elacestrant (Orserdu, Stemline Therapeutics, Inc).

The new therapy, a selective estrogen receptor down regulator (SERD), is indicated for the treatment of postmenopausal women or adult men with estrogen receptor-positive/HER2-negative ESR1-mutated advanced or metastatic breast cancer who have been treated unsuccessfully with at least one previous endocrine therapy. The FDA approved the therapy in January.

Meeting a need

Elacestrant is the only SERD for oral use. McDonnell says it fills a significant unmet need because up to 40% of patients diagnosed with ER-positive/HER2-negative breast cancer will acquire ESR1 mutations as the cancer advances. In most cases, these mutations will trigger resistance to standard endocrine therapies.

During the past decade, the McDonnell Lab has been focused on identifying and developing new endocrine therapies to treat advanced ER-positive breast cancer. This initiative has included revisiting older hormone therapies originally developed to treat osteoporosis or menopause symptoms.

Elacestrant, for example, was developed initially to treat hot flashes in post-menopausal women but was never approved for that use. Clinical trials demonstrated that RAD1901, as the therapy was known, stopped hot flashes at low doses but increased them at higher doses. McDonnell and researchers in his lab were intrigued by the pharmacology. “It turns out that the reason for RAD1901’s failure as a treatment for hot flashes was a useful property for a breast cancer drug,” says McDonnell."

McDonnell Lab investigators Suzanne E. Wardell, PhD, and Erik Nelson, PhD, determined that RAD1901 was effective at blocking the estrogen driving cancer cell growth by binding to its receptor, like a selective estrogen receptor modulator (SERM), and degrading the estrogen receptor, like a SERD.

Wardell and Nelson went on to demonstrate that RAD1901 inhibited tumor growth in mouse models. This was the springboard for continued investigations worldwide; culminating in the successful multicenter phase 3 clinical trial (EMERALD 2018-2022) that led to FDA approval.

Accessing elacestrant

“We’re already prescribing elacestrant for our patients,” says Heather N. Moore, PharmD, BCOP, CPP, clinical oncology pharmacist with DCI’s breast group, noting that the drug is currently being distributed nationally by two specialty pharmacies. Duke Health does not distribute the drug.

Moore also reminds providers that elacestrant is indicated only in ER-positive/HER2-negative ESR1-mutated breast cancer and that it’s a monotherapy. It is not approved for clinical use in combination with other cancer therapies.

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