RxPONDER trial will evaluate whether gene expression test can drive chemotherapy choice

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Cancer researchers at hundreds of sites nationwide are about to launch a SWOG-led clinical trial that could keep thousands of breast cancer patients from getting chemotherapy that is unlikely to do them any good.

Each year in the United States more than 60,000 women are diagnosed with hormone receptor-positive breast cancer that has spread to their lymph nodes. Almost all get chemotherapy in addition to endocrine therapy, but analyses of earlier studies have suggested that the two-thirds of these women with the lowest Oncotype DX recurrence scores may see little or no benefit from that chemotherapy.

The RxPONDER (Rx for Positive Node, Endocrine Responsive Breast Cancer) trial will reveal whether chemotherapy benefits patients with node positive breast cancer who have low to intermediate Oncotype DX recurrence scores. The trial also seeks to determine whether there is an optimal recurrence score cutpoint for these patients, above which chemotherapy should be recommended.

"If the RxPONDER trial confirms findings from earlier studies," says study coordinator Ana M. Gonzalez-Angulo, M.D., of the MD Anderson Cancer Center, "it will mean that we know more precisely how to use a genomic-based test to spare thousands of women whose breast cancer has spread to as many as three lymph nodes the grueling side effects and staggering costs of chemotherapy they don't need."

The Oncotype DX assay costs about $4,000 per patient, yet the chemotherapy treatment now routinely given to these patients costs more than $20,000 per course, meaning that the results of the RxPONDER study could also save hundreds of millions of dollars in health care costs each year.

Researchers plan to enroll 4,000 women with recurrence scores of 25 or less who have early stage, hormone receptor-positive, HER2-negative breast cancer that has been found to involve one to three lymph nodes. They expect to screen about 9,000 breast cancer patients in order to register these 4,000, who will be randomized to receive either chemotherapy with endocrine therapy or endocrine therapy alone.

The phase III trial is being led by SWOG, one of the largest of the National Cancer Institute supported clinical trial cooperative groups, but is expected to be opened by the other major cooperative groups as well, giving patients almost anywhere in the United States access to the trial.

Patients can see a list of sites where the trial is currently open by going to swog.org/RxPONDER or can ask their doctor about the trial.

The Oncotype DX test measures the expression, or activity, level of 21 specific genes within a tumor sample and based on that pattern assigns a recurrence score of anywhere from 0 to 100. Earlier trials have shown that the higher the recurrence score, the more likely the patient's cancer will recur. The assay is performed by Genomic Health, Inc., based in Redwood City, California.

Oncotype DX is only one of several gene expression profile tests oncologists now use to help them judge how likely it is a patient's cancer will return or to inform treatment decisions. RxPONDER researchers plan to evaluate other tests as well, including the PAM50 test, which measures the expression level of a set of 50 genes to determine a

patient's "risk of recurrence" score.

"There are larger questions here," says Laurence H. Baker, D.O., SWOG group chair and professor of internal medicine and pharmacology at the University of Michigan. "Can lab tests allow us to target follow-up chemotherapy in a much narrower and more effective way? And if so, which tests are most clinically effective for our patients and most cost effective?"

The TAILORx trial in node-negative breast cancer (cancer that has not spread to the patient's lymph nodes), which recently enrolled its final patient, used the Oncotype DX assay to select patients with mid-range recurrence scores for study, and will help identify in which of these patients adjuvant endocrine therapy alone is sufficient treatment. Final results of the TAILORx trial will not be known for several years.

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