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Genomic test shows promise as chemotherapy response, survival predictor for women with breast cancer

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A new genomic test combining multiple signatures – a patient's estrogen receptor status, endocrine therapy response, chemotherapy resistance and sensitivity – shows promise as a predictor of chemotherapy response and survival benefit in women with invasive breast cancer, according to research led by The University of Texas MD Anderson Cancer Center.

The findings, published in the May 11 issue of *JAMA*, also may determine those for whom standard therapy alone might not offer enough, and/or for whom an appropriate clinical trial in the adjuvant setting could provide additional benefit.

"The research builds on a decade of collaborative work in developing a clinically meaningful chemotherapy predictor, and, if validated in future studies, could guide therapy for about 80 percent of newly diagnosed women with invasive breast cancer who are candidates for chemotherapy," says W. Fraser Symmans, MD, professor in MD Anderson's Department of Pathology.

"The test helps us understand both resistance and response to chemotherapy more specifically, how sensitivity to endocrine therapy would impact a predictor and how to focus on specific subtypes of breast cancer – in this case HER2 negative disease stratified by estrogen receptor (ER) status – because we've learned that they are so intrinsically different," Symmans continues.

The multicenter study enrolled 310 Stage II and III newly diagnosed women with invasive breast cancer (discovery cohort). All were Her2 negative and received the chemotherapy regimen of sequential taxane and anthracycline, followed by endocrine therapy, if hormone receptor positive. Gene expression microarrays from the discovery cohort were used to develop different predictive signatures for drug resistance and response. Using the signatures for endocrine therapy response, chemotherapy resistance and sensitivity, in combination with other genomic predictors to chemotherapy response, breast cancer treatment was predicted in an independent cohort of 198 breast cancer patients with similar diagnosis and treatment (independent cohort).

The study's primary endpoint was distant relapse-free survival (DRFS) and absolute risk reduction (ARR) and the median follow up was three years. Excluding women with known endocrine sensitivity, the algorithm had a positive predictive value (PPV) of 56 percent. In the 28 percent who were predicted treatment-sensitive, their three-year DRFS was 92 percent, ARR was18 percent and they had a five-fold reduction of risk of distant relapse.

When analyzed by ER status, treatment sensitivity was predicted in 30 percent of the ER-positive women and in 26 percent of those who were ER-negative. At three year follow up, DRFS and ARR was 97 percent and 11 percent, respectively, in the ER-positive cohort, compared to 83 percent and 26 percent, respectively, in the ER-negative cohort.

"From a therapeutic standpoint, we know that the treatment a patient receives at initial diagnosis offers the greatest chance for cure. At the same time, we have many potential clinical trials with novel therapeutics and targeted agents in breast cancer. Currently, we're still not sure who we are curing with chemotherapy and who also could benefit from these novel therapies," says Lajos Pusztai, M.D., D.Phil, professor in the Department of Breast Medical Oncology and an author on the study.

If validated in future studies, these findings could be used as a treatment gatekeeper, explains Pusztai, guiding women and their physicians by affirming the selection of standard chemotherapy or, for those at greater risk for recurrence, to a potentially therapeutic clinical trial in the adjuvant setting, from which they may gain further clinical benefit.

More information: *JAMA*. 2011;305[18]1873-1881.