Mayo collaboration finds source of breast drug side effect

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Mayo Clinic researchers and their international colleagues have discovered genetic variants that lead to severe arthritis for a subset of women when taking aromatase inhibitors to treat their breast cancer. This serious side effect is so painful that many women halt their lifesaving medication. The findings appear today in the online issue of *Journal of Clinical Oncology*.

"Many women stop taking aromatase inhibitors due to the accompanying joint pain," says James Ingle, M.D., Mayo Clinic oncologist and senior author of the study. "We used the latest genetic technology in a very large group of women and discovered totally new clues to the cause of the main reason women stop this potentially lifesaving drug. Our findings open the door to finding ways to identify women who will develop these side effects and treat those who do, thus allowing more women to take this therapy and decrease their chances of breast cancer recurrence." Aromatase inhibitors are most often used as adjuvant therapy for postmenopausal women with early stage breast cancer.

How the Research Was Conducted

The researchers -- including investigators from the United States, Canada and Japan -- conducted a genome-wide association study to identify gene variants called single nucleotide polymorphisms (SNPs) that are associated with musculoskeletal pain. They selected patients who were enrolled in a prospective clinical trial, MA27, conducted by the

NCIC Clinical Trials Group in Canada in collaboration with the NCI-sponsored North American Breast Cancer Groups comparing two aromatase inhibitor drugs. Two controls were matched with each patient and each patient who was selected experienced arthritis-like side effects within the first two years of treatment, or had already dropped out of the trial because of the pain. Researchers studied 293 separate cases, comparing them to 585 controls.

They found four likely SNPs on chromosome 14, all of which were nearest the gene T-Cell Leukemia 1A, which they discovered also was estrogen dependent. One of the SNPs also created an estrogen response with increased gene expression after exposure to estradiol, a widely used post-menopausal treatment. The results provide researchers with genetic markers for the aromatase inhibitor-induced arthritis and clues to find ways to treat it.

Provided by Mayo Clinic