Novel agent set for unique clinical test in inflammatory breast cancer

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A drug now used to treat a type of lymphoma has shown surprising benefit in preclinical studies of inflammatory breast cancer, according to a researcher at Thomas Jefferson University's Kimmel Cancer Center.

The finding, published online this month in the *Journal of Experimental Therapeutics and Oncology*, has led to development of a phase 1/2 clinical trial at Kimmel Cancer Center to test the agent, Romidepsin (Istodax), in combination with nab-paclitaxel (Abraxane) chemotherapy for advanced inflammatory breast cancer (IBC).

"Because this kind of breast cancer is very difficult to treat, we hope this new combination of anticancer agents will change the outcome of this aggressive disease," says the study's senior investigator, Massimo Cristofanilli, M.D., F.A.C.P., Professor of Medical Oncology and Director of the Jefferson Breast Care Center.

The study was conducted in collaboration with the lead author, Fredika Robertson, Ph.D., at The University of Texas M. D. Anderson Cancer Center, and was supported by a Promise Grant from the Susan G Komen Foundation awarded to Drs. Cristofanilli and Robertson in 2008.

Inflammatory breast cancer (IBC) is the most metastatic variant of locally advanced breast cancer, Dr. Cristofanilli says. Although it accounts for between 2-5 percent of all breast cancers in the United States—and 13 percent of breast cancers globally—it is responsible for a disproportionate number of deaths from breast cancer, he says.

One of the reasons for the lethality of inflammatory breast cancer is that early in the disease onset it produces emboli—small balls of cancer cells—which spread through the lymph system causing the typical breast swelling. These aggregates of cancer cells are resistant to chemotherapy, radiation, and are believed to be responsible for rapid metastasis, Dr. Cristofanilli says.

Experiments in laboratory cells and in mice models of inflammatory breast cancer demonstrates that Romidepsin is able to break the bonds that bind the cancer cells together, which then allows chemotherapy to effectively target single cancer cells, he says.

Romidepsin is a histone deacetylase (HDAC) inhibitor, a new class of drugs that regulates gene transcription in a unique way.

This study tested two other HDAC inhibitors, but found Romidepsin offered the best results. The agent was approved for use to treat cutaneous T-cell lymphoma in 2009. It is also undergoing clinical trials for use in other lymphomas.

"This study is a nice example of a transition from the laboratory to the clinic," says Dr. Cristofanilli. "Our laboratory work suggested it might be helpful to treat inflammatory breast cancer, and now we are about to open a clinical trial to test that very promising possibility."

Provided by Thomas Jefferson University