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Addition of dasatinib to standard chemo cocktail may enhance effect in certain ovarian cancers

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The addition of a chemotherapeutic drug for leukemia to a standard regimen of two other chemotherapy drugs appears to enhance the response of certain ovarian cancers to treatment, according to a pre-clinical study led by researchers in the Duke Comprehensive Cancer Center.

"We know that a pathway called SRC is involved in cell proliferation in certain types of cancers, including some ovarian cancers," said Deanna Teoh, M.D., a fellow in gynecologic oncology at Duke and lead investigator on this study. "By examining gene expression data, we determined that the combination of the leukemia drug dasatinib (Sprycel) made carboplatin and paclitaxel more effective in cell lines with higher levels of SRC expression and SRC pathway deregulation."

That synergistic effect, in which drugs used in combination strengthen each other's efficacy, was absent when low SRC expression and low SRC pathway deregulation were present, Teoh said.

"These findings indicate that we may be able to direct the use of a targeted therapy like dasatinib based on gene expression pathways in select ovarian cancers," she said.

The results of the study are being presented on a poster at the 100th annual American Association for Cancer Research meeting in Denver on

April 19, 2009. The study was funded by the Prudent Fund and the National Institutes of Health.

"Our ultimate goal is to offer personalized therapy for women with ovarian cancer," said Angeles Secord, M.D., a gynecologic oncologist at Duke and senior investigator on this study. "Hopefully in the future we will apply targeted therapies to individual patients and their cancers in order to augment response to treatment while minimizing toxic side effects."

For this study, researchers examined four ovarian cancer cell lines, known as IGROV1, SKOV3, OVCAR3 and A2780. Three of the cell lines demonstrated high activation of SRC and one demonstrated lower SRC expression. All were treated in lab dishes with various combinations of the chemotherapeutic agents dasatinib, carboplatin and paclitaxel.

"We found that the addition of dasatinib to standard therapy in the three cell lines with significant SRC pathway deregulation - IGROV1, OVCAR3 and A2780 - enhanced the response of the cancer cells to therapy," Teoh said. "Conversely, in SKOV3, which has minimal SRC protein expression and pathway deregulation, we saw the least amount of anti-cancer activity when we added dasatinib."

It's possible that by blocking the SRC activity with the dasatinib, we are enhancing the effect of the other chemotherapeutic agents, Teoh said.

The results of this study support the further investigation of targeted biologic therapy using a SRC inhibitor in some ovarian cancers, she said. Currently a phase I trial of a combination of dasatinib, paclitaxel and carboplatin is available for women with advanced or recurrent ovarian, tubal and peritoneal cancers.

Dasatinib is a chemotherapeutic that is currently FDA-approved for use in leukemia. It is manufactured by Bristol-Myers Squibb and is sold under the brand name Sprycel. Bristol-Myers Squibb provided the dasatinib used in this study.

Other researchers involved in this study include Tina Ayeni, Jennifer Rubatt, Regina Whitaker, Holly Dressman and Andrew Berchuck.

Source: Duke University Medical Center (news : web)