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FDA approved leukemia drugs shows promise in ovarian cancer cells

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The drug Sprycel, approved for use by the U.S. Food and Drug Administration in patients with chronic myeloid leukemia, significantly inhibited the growth and invasiveness of ovarian cancer cells and also promoted their death, a study by researchers with UCLA's Jonsson Comprehensive Cancer Center found.

The drug, when paired with a chemotherapy regimen, was even more effective in fighting ovarian cancer in cell lines in which signaling of the Src family kinases, associated with the deadly disease, is activated.

The study appears in the Nov. 10, 2009 edition of the *British Medical Journal*.

Ovarian cancer, which will strike 21,600 women this year and kill 15,500, causes more deaths than any other cancer of the female reproductive system. Few effective therapies for ovarian cancer exist, so it would be advantageous for patients if a new drug could be found that fights the cancer, said Gottfried Konecny, an assistant professor of hematology/oncology, a Jonsson Cancer Center researcher and first author of the study.

"I think Sprycel could be a potential additional drug for treating patients with Src dependent ovarian cancer," Konecny said. "It is important to remember that this work is only on cancer cell lines, but it is significant enough that it should be used to justify clinical trials to confirm that women with this type of ovarian cancer could benefit."

Recent gene expression studies have shown that about one-third of women have ovarian cancers with activated Src pathways, so the drug could potentially help 7,000 ovarian cancer patients every year.

In this study, the UCLA team tested the drug against 34 ovarian cancer cell lines and they conducted genetic analysis on all cell lines. Through these analyses, the researchers were able to identify genes that predict response to Sprycel. If the work is confirmed in human studies, it may be possible to test patients for Src activation and select those who would respond prior to treatment, personalizing their care.

"We were able to identify markers in the pre-clinical setting that would allow us to predict response to Sprycel," Konecny said. "These may help us in future clinical trials in selecting patients for studies of the drug."

Sprycel is what is known as a "dirty" kinase inhibitor, meaning it inhibits more than one pathway. Konecny said it also inhibits the focal adhesion kinase and ephrin receptor, also associated with ovarian cancer.

The next step, Konecny said, would be to test the drug on women with ovarian cancer in a clinical trial. The tissue of responders would then be analyzed to determine if the Src and other pathways were activated. If that is confirmed, it would further prove that Sprycel could be used to fight ovarian cancer. In studies, women would be screened before entering a trial and only those with Src dependent cancers could be enrolled to provide further evidence, Konecny said, much like the studies of the molecularly targeted breast cancer drug Herceptin enrolled only women who had HER-2 positive disease.

"Herceptin is different because we knew in advance that the only worked in women with HER-2 amplification," he said. "In this case, we don't clearly know that yet. The data reassure us that the drug works where the targets are over-expressed but we need more testing to confirm this."

The tests combining the drug with chemotherapy are significant because chemotherapy currently is the first line treatment for ovarian cancer patients following surgery. Because Sprycel proved to have a synergistic effect when combined with chemotherapy - both made the other work better - it may be possible to add the targeted therapy as a first line treatment if its efficacy is confirmed in future studies, adding a new tool to an oncologist's arsenal.

Source: University of California - Los Angeles