Researchers find drug duo kills chemotherapy-resistant ovarian cancer cells

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The use of two drugs never tried in combination before in ovarian cancer resulted in a 70 percent destruction of cancer cells already resistant to commonly used chemotherapy agents, say researchers at Mayo Clinic in Florida. Their report, published online in *Gynecologic Oncology*, suggests that this combination (ixabepilone and sunitinib), might offer a much needed treatment option for women with advanced ovarian cancer. When caught at late stages, ovarian cancer is often fatal because it progressively stops responding to the chemotherapy drugs used to treat it.

"Women die from ovarian cancer because their tumors become resistant to chemotherapy, so a drug that might be able to reduce that resistance — which may be what this combination of agents is doing — would be a boon to treatment of this difficult cancer," says study co-author Gerardo Colon-Otero, M.D., a hematologist-oncologist who cares for ovarian cancer patients.

The finding also highlights the importance of the role of a molecule, RhoB, that the researchers say is activated by the drug duo. The study's senior investigator, cancer biologist John Copland, Ph.D., has identified RhoB as a key modulator for drug response in other tumor types, but says its role in ovarian cancer was unknown before this study.

"Now we find that with this combination of drugs, RhoB is increased and cells die," he says.

The study was possible because Dr. Copland and his laboratory colleagues, including co-author Laura Marlow, created and characterized two new ovarian laboratory cell lines. They were derived from tumor tissue specimens taken from a patient with metastatic cancer whose tumors had stopped responding to multiple chemotherapy drugs.

Dr. Colon-Otero suggested trying the two drugs on the new cells lines. Neither drug is approved for use in ovarian cancer. Ixabepilone is a chemotherapy drug that, like other taxane drugs, targets the microtubules and stops dividing cells from forming a spindle. It has been approved for use in metastatic breast cancer. Sunitinib, approved for use in kidney cancer, belongs to a class of tyrosine kinase inhibitors that stops growth signals from reaching inside cancer cells.

Prakash Vishnu, M.D., a former fellow at Mayo Clinic in Florida who is now at the Floyd and Delores Jones Cancer Institute in Virginia Mason Medical Center, Seattle, is the first author of the article and led the study under the mentorship of Drs. Colon-Otero and Copland. He found that in both cell lines, cell kill was significantly greater with the combination than use of either drug alone. For example, in chemotherapy-resistant lines (where this potential combination therapy will most likely be used), ixabepilone alone killed up to 30 percent of cells, and the rate for suntinib was up to 10 percent. When the agents were used together, the kill rate was 70 percent.

Dr. Copland said that RhoB is a potential biomarker that may help identify patients who might benefit from such combination therapy.

Provided by Mayo Clinic

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