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Two-drug combination may slow deadly thyroid cancer

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A combination of the drugs pazopanib and paclitaxel shows promise in slowing anaplastic thyroid cancer (ATC), according to a Mayo Clinic-led study published in the journal *Science Translational Medicine*. The two drugs together resulted in greater anti-cancer activity in ATC than either drug alone, says lead researcher Keith Bible, M.D., Ph.D., a Mayo Clinic oncologist.

Anaplastic thyroid cancer is a rare but devastating form of thyroid cancer that typically strikes men and women in their 60s and 70s. It is very aggressive, with a median survival of only about 5 months from time of diagnosis. Only 20 percent of patients survive a year beyond diagnosis, and it has historically been found to be resistant to most therapies.

Pazopanib, a kinase-inhibitor that interferes with the growth of cancer cells, is already approved by the Food and Drug Administration (FDA) to treat renal cancer tumors. Paclitaxel is an FDA-approved chemotherapy drug that disrupts the machinery involved in cell division.

Researchers studied anaplastic thyroid cancer cells and tumors in cell culture and in animal models. Human ATC cells were readily killed, and ATC tumors implanted into mice were 50 percent smaller when treated with the combination in comparison to the response to treatment with either drug alone. Pilot therapy of one patient with metastatic anaplastic thyroid cancer using the combination also resulted in marked tumor shrinkage lasting over six months. "This was a highly unexpected finding

for this type of aggressive tumor, which often can double in size in a matter of days," Dr. Bible says.

In previous studies, pazopanib alone was found not effective in the treatment of anaplastic thyroid cancer. Paclitaxel was added to address the aggressiveness of anaplastic thyroid cancer tumors and bolster anti-cancer effects. The team investigated how the two drugs might complement each other.

Monitoring cancer cells multiply in time-lapse video under a microscope, researchers noted that the drug combination resulted in abnormal cell division and an increase in ATC cell death. Although pazopanib had not been known to specifically affect cell division, researchers speculated that the drug might have another unrecognized molecular target within cancer cells.

"We ended up learning that pazopanib also happens to inhibit a protein involved in cell division known as aurora A; this property seems to be involved in producing enhanced effects when pazopanib is combined with paclitaxel," Dr. Bible says. "This finding suggests that the combination may also be useful in treating other cancers, such as breast cancer, in which aurora A is sometimes found to be present in elevated amounts, as it is in ATC," Dr. Bible says.

The results also prompted an ongoing randomized multicenter clinical trial, led by Mayo Clinic and Memorial Sloan-Kettering Cancer Center and administered through the Radiation Therapy Oncology Group, testing the two-drug combination when added to radiation therapy in the initial treatment of patients with anaplastic thyroid cancer.

"This important next step is designed to determine whether the combination of drugs will improve ATC patient survival compared to paclitaxel alone," Dr. Bible says.

More information: The research was funded by National Institutes of Health grants CA125750 and CA13666 and the State of Florida Department of Health Bankhead-Coley Cancer Program.

Provided by Mayo Clinic

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