Study to treat deadly form of thyroid cancer shows promise, researchers say

April 19 2013

(Medical Xpress)—A combination of therapies may prove to be a promising advance for the treatment of anaplastic thyroid cancer based on results of a phase I clinical trial, say researchers at Mayo Clinic in Florida.

Anaplastic thyroid cancer is one of the deadliest of all cancers. Nearly all patients diagnosed with this cancer die from it, and life expectancies are measured in weeks to a few months. Even though it is very rare—approximately 600 patients are diagnosed with anaplastic thyroid cancer each year in the United States—the cancer accounts for 50 percent of all deaths from all types of thyroid cancer, according to the American Thyroid Association.

The collaborative study, published in the April 16 online issue of the *Journal of Clinical Endocrinology & Metabolism*, reports that combining paclitaxel chemotherapy with an experimental agent known as efatutazone was safe and well tolerated by patients. Efatutazone in combinatorial therapy is also being studied in clinical trials for colon and lung cancers.

"This is good news, because we did not reach a maximum tolerated dose, meaning that the drug is well tolerated," says the study's lead investigator, Robert Smallridge, M.D., an endocrinologist who treats patients with thyroid cancer.

But he added that the study of 15 patients, most of whom were at the

most advanced metastatic stage, also demonstrated "a trend toward clinical benefit."

One patient had a partial response, defined as a greater than 30 percent reduction in the size of tumors, and seven patients experienced short-term stable disease, meaning a period when the tumors did not grow.

If correct, these are just glimpses of treatment benefit, and a phase II clinical trial is needed to define a true clinical advantage, says Dr. Smallridge. But any hint of progress in treating this deadly cancer is heartening, he adds.

"To see a partial response is very rare in anaplastic thyroid cancer," Dr. Smallridge says.

The study found that doubling the dose of efatutazone (from 0.15 mg daily to .03 mg daily) delayed the median time to progression from 48 days to 68 days, and pushed median survival from 98 days to 138 days, respectively.

"We are encouraged that this drug combination showed biologic activity in this deadly disease and feel that additional testing with this and other new agents will be helpful in trying to improve outlook and outcome for patients," says Dr. Smallridge.

Efatutazone is a PPAR-gamma activator which turns on a powerful tumor suppressor capable of halting cell growth, says Mayo Clinic in Florida cancer biologist John Copland, Ph.D., a study co-author. PPAR-gamma is a transcriptional factor that increases the expression of many genes, and Dr. Copland's early work on the agent showed that it forces PPAR-gamma to turn on two tumor suppressor genes that have been silenced in anaplastic thyroid cancer. "It is very rare that a drug can take a suppressed gene and cause it to be re-expressed," he says.

Provided by Mayo Clinic