Clinical trial of experimental drug targeting mutation in thyroid cancer shows clinical benefit

by Mary Ruth Helms — last modified Apr 02, 2012 04:42 PM

Chapel Hill - In a clinical trial of an experimental drug to treat thyroid cancer, UNC and six other institutions report the first evidence in this tumor that targeting therapy to an oncogene documented to be present in the patient receiving therapy may be associated with clinical benefit.

Neil Hayes, MD, is the UNC principal investigator and first author of the study.

UNC scientists partnered in a clinical trial using the experimental drug selumetinib to treat advanced cases of the most common type of thyroid cancer called papillary thyroid cancer. Selumetinib targets and blocks the molecular pathway by which an oncogene called BRAF is activated. Up to 50 percent of thyroid cancers harbor this single gene alteration-called BRAF mutation- that is blocked by the drug.

In the trial, patients' tumors were tested to confirm the mutation, and therapy was begun. Patients with the mutation who took the drug tolerated it well and patients without the mutation had no clinical benefit from the drug.

"We investigated the safety and effectiveness of selumetinib in patients with advanced thyroid cancer and found that in patients without the BRAF mutation the drug showed no evidence of activity. However, when we focused the evaluation to the 50 percent patients with the abnormal gene, we saw striking differences in the patient responses," says Neil Hayes, MD, MPH, the UNC principal investigator and first author of the study. Because of the small size of the trial, this observation requires additional studies, but has powerful implications for the design of future studies and the drugs that should be considered. Hayes is associate professor of medicine and a member of UNC Lineberger Comprehensive Cancer Center.

"We feel this provides the first evidence in thyroid cancer that targeting this commonly altered pathway may have resulted in benefit for only the patients whose tumors demonstrated the mutation. When speaking about personalized cancer therapy, this is the kind of example we are looking for." Their results were published in the April 1, 2012 issue of the journal Clinical Cancer Research.

The Phase 2 trial involved 39 patients with iodine-refractory papillary thyroid cancer for which there are few therapeutic options and no consensus standard of care. Radioactive iodine therapy is one treatment for papillary thyroid cancer when patients are given a large dose of the substance, killing thyroid cells and the cancer.

The only FDA approved drug to date used to treat the advanced stage of disease isn't always beneficial and has many side effects. A number of newer drugs have shown striking promise, but these work through a different mechanism and FDA approval is generally still pending.

Thyroid cancer incidence is increasing, rising 5 to 6 percent annually. The most common type is papillary, comprising 70 to 80 percent of the cases. Although the prognosis is very good for papillary thyroid cancer if detected early with an overall 10-year survival rate of 98 percent, once the cancer is locally advanced or metastatic or no longer amenable to surgery, the survival rate declines.

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