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Trial seeks 'genetic fingerprint' for predicting drug effectiveness

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University of Cincinnati (UC) physician-scientists believe identifying a genetic “fingerprint” could help predict which specific therapies will be most effective for patients with gastric cancer.

Syed Ahmad, MD, is leading a national, phase-2 trial to test the effectiveness of combined chemotherapy and radiation therapy given to patients with gastric cancer before surgery. His team will also collect biological samples in an attempt to obtain genetic data that could be used to formulate targeted therapies.

Previous studies have established that either chemotherapy or radiation therapy after surgery can improve patient survival compared with surgery alone. Overall survival rates, however, remain low—with 20 to 30 percent of American patients surviving more than five years after treatment.

“Everyone agrees that without surgery, gastric cancer in not curable, and numerous studies have shown a benefit to follow-¬up therapy with either chemotherapy or radiation therapy,” says Ahmad, assistant professor of surgery at UC and principal investigator of the trial.

“The problem is you can’t give both radiation therapy and chemotherapy after surgery—it’s too toxic and patients can’t tolerate it,” he says. “But you can give it before surgery when patients are healthiest.”

This trial addresses what Ahmad calls the “future of cancer therapy”:

targeted drug regimens, based on the characteristics of a patient's specific tumor.

His goal is to identify a genetic "fingerprint" that could help predict whether patients will respond to therapy, and then identify drugs to address the specific molecular characteristics of that patient's tumor.

"Right now treatment is based on the assumption that site-based cancers are all the same, so every patient who has stage-3 gastric cancer will get the same chemotherapy drugs," Ahmad explains. "But the reality is that every cancer has a different expression of hormones, growth factors and genetic factors that must be addressed individually.

The UC-led national team is looking for about 70 patients across the United States with up to stage-3 gastric cancer to participate in the trial.

Prior to surgery, all study participants will have a biopsy to set baseline standards for genetic testing to determine which patients have a complete response to the multi-treatment therapy. Participants will receive daily doses of the platinum-containing drug oxaliplatin (ox-AL'-ih-plah-tin, marketed as Eloxatin) for six to eight weeks.

Approved by the Food and Drug Administration, oxaliplatin is currently used to treat advanced colorectal cancer. Studies have shown the drug has fewer toxicity complications compared with other therapies.

After six weeks of chemotherapy, the patient will get five consecutive days of three-dimensional, external-beam radiation therapy. Patients will be reevaluated two to three weeks after radiation to determine if they are eligible for surgery. Those who are suitable will have another tissue biopsy after surgery.

Researchers will compare pre- and post-surgery tissue samples to obtain

the genetic data necessary to establish associations between molecular markers and drug resistance, with the goal of reducing toxicity associated with chemotherapeutic agents and improving patient survival.

Source: University of Cincinnati