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Phase I study of temsirolimus, capecitabine proves safe; positive survival trend seen

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A phase I clinical trial examining the safety of combining temsirolimus and capecitabine in advanced malignancies suggests the two agents can be given safely to patients. In addition, the Georgetown Lombardi Comprehensive Cancer Center researchers conducting the study in cancer patients whose tumors have resisted multiple treatments say the combination demonstrates "promising evidence" of disease control and should be studied in a phase II trial. Their clinical findings and additional data from the study will be presented at the American Society of Clinical Oncology (ASCO) annual meeting in Chicago, June 1 through 5, 2012.

Temsirolimus is an mTOR inhibitor, meaning it stops mTOR from doing its job inside a cell. mTOR controls parts of a cell's machinery, including the production of proteins, and it is essential for cancer cell growth. However, researchers know it's not enough to stop one cellular mechanism in the vast majority of cancers. They hypothesize that by adding a chemotherapy, capecitabine, to temsirolimus, the combination will overwhelm the cancer cells and cause them to die.

Thirty-two patients with advanced cancers volunteered to participate in the phase I study of temsirolimus and capecitabine. The men and women had received an average of four previous types of treatments. The study was designed to examine the safety of various combination doses among the patients. Side effects were assessed in 30 patients.

The most common adverse events were mucositis (inflammation and ulceration of the mucous membranes lining the digestive tract), and

hypophosphatemia (low level of phosphorus in the blood causing bone pain, confusion and muscle weakness). The most common serious adverse events were fatigue (4), diarrhea (2) and hypophosphatemia (2). For 16 of 30 patients, the dose of capecitabine was lowered to help alleviate side effects.

Of the 25 patients evaluable for the effectiveness of the combination, there were no partial responses or complete responses observed, but 14 patients had stable disease (no growth) – some with stable disease for more than six months. The median time to progression was three months with a median overall survival of seven months.

"We're not surprised by the safety profile of this combination," says the principal investigator, Michael Pishvaian, M.D., Ph.D., a gastrointestinal cancer specialist at Georgetown Lombardi. "While phase I studies are not designed to measure the tumor's response to a drug or combination of drugs, it is encouraging when we see some clinical benefit. Looking ahead, I anticipate this combination will be studied in phase II trial for colon cancer patients who have exhausted all options for treatments."

Provided by Georgetown University Medical Center