Blood test could guide treatment for kidney cancer

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A common enzyme that is easily detected in blood may predict how well patients with advanced kidney cancer will respond to a specific treatment, according to doctors at Duke Cancer Institute.

The finding, published online Monday, Aug. 13, 2012, in the Journal of Clinical Oncology, could lead to the first blood test to determine the best treatment for late-stage kidney cancer.

"Being able to direct these patients to a treatment we know will help them would be a major advancement in their care," said Andrew Armstrong, M.D., ScM, associate professor of medicine and surgery at Duke and lead author of the study. "At the same time, patients who would not benefit from the treatment would be spared from undergoing a drug regimen with potential side effects that could diminish their quality of life."

If further studies verify the initial results, the finding could change how doctors treat patients for a disease that has been increasing in the United States. The National Cancer Institute estimates kidney cancer will strike 65,000 people in the U.S. this year, and almost 14,000 will die of the disease.

Armstrong and colleagues at Duke focused on an enzyme known as lactate dehydrogenase, or LDH, which is found in almost all body tissues and plays a role in converting food to energy. As cells die or are injured, they release LDH, so elevated levels of the enzyme have long been used

in blood tests to identify cancer, tissue damage, and other disorders.

In kidney cancer, elevated LDH levels have been considered a risk factor for aggressive disease, signaling tumor progression. More recent studies have suggested that elevated LDH may also indicate the activation of key genetic alterations that lead to cancer proliferation. One of these cancer gene pathways relies on a protein called mammalian target of rapamycin, or mTOR, and drugs called mTOR inhibitors work to shut down the process.

An international Phase III trial testing an mTOR inhibitor known as temsirolimus found that the then-investigational drug extended the lives of patients with kidney cancer that had spread to other areas of the body, and it even helped the patients with high LDH levels who typically have a poor prognosis.

Intrigued by those results, the Duke researchers used data from the trial to determine whether a high LDH level was more than just a prognostic tool in advanced kidney cancer, and could perhaps also predict the effectiveness of an mTOR inhibitor.

Armstrong and colleagues analyzed the outcomes of 404 of the study participants, approximately half of whom received a standard therapy, interferon-alpha, and half who received temsirolimus, which has since been approved by the U.S. Food and Drug Administration to treat kidney cancer. LDH levels had been measured at the start of the study for all participants.

In their analysis, the Duke team found that patients with high LDH levels at the start of the study survived significantly longer on the mTOR inhibitor drug than they did on interferon-alpha. Median survival for patients with high LDH levels was 6.9 months on temsirolimus compared to 4.2 months for the high LDH level patients on the standard

drug. At six months, 53.7 percent of high LDH level patients taking temsirolimus were alive, compared to 39.5 percent taking interferon-alpha. Patient survival rates at 12 months were 34.3 percent for temsirolimus, vs. 12.7 percent for interferon-alpha.

Patients with low LDH at the start of the study showed little difference in survival based on the drug they received, with median survival of 11.7 months for the mTOR inhibitor patients compared to 10.4 months for those taking interferon-alpha.

"This is an exciting finding," Armstrong said. "In breast cancer, for example, we can test for HER-2 expression and offer effective treatments based on that. Having a similar biomarker for kidney cancer that could direct patients to the best therapies for their cancer would be a major step forward."

Armstrong said additional studies are needed to verify the finding, and to determine whether LDH might predict the success of additional drugs that target other cancers.

Provided by Duke University Medical Center