Widely used kidney cancer drugs can't stop recurrence

March 10 2016, by Steve Graff

Two widely used targeted therapy drugs approved by the FDA for the treatment of metastatic kidney cancer—sorafenib and sunitinib—are no more effective than a placebo in preventing return of the disease to increase life spans of patients suffering from advanced kidney cancer after surgery, according to a new multi-institutional study in the Lancet led by a researcher at the Abramson Cancer Center (ACC) of the University of Pennsylvania.

Naomi B. Haas, MD, an associate professor in the division of Hematology/Oncology at the Perelman School of Medicine and director of the Prostate and Kidney Cancer Program at the ACC, and her colleagues in the ECOG-ACRIN Cancer Research Group (ECOG-ACRIN), treated 1,943 patients in the United States and Canada with one year of sorafenib, sunitinib, or a placebo drug after surgery to remove their kidney tumors. The study found no difference in median years of disease-free survival in the adjuvant setting (post-surgery): 5.8 years for sunitinib; 6.1 years for sorafenib; and 6.6 years for placebos.

Although the study did not establish a role for the drugs in the adjuvant setting, it has provided a definitive answer about their use that will help prevent any associated costs and toxic effects.

Preliminary results of this randomized, double-blind phase III trial, known as ASSURE, were presented last year during the American Society of Clinical Oncology 2015 Genitourinary Cancers Symposium.

The study involved patients and researchers from 226 centers, including Massachusetts General Hospital and the Dana Farber Cancer Institute. Robert Uzzo, MD, chair of Surgery, and Yu Ning Wong, MD, an associate professor of Medicine, at Fox Chase Cancer Center—Temple Health in Philadelphia, served as co-authors.

While surgery is typically the best initial treatment for renal tumors, surgical resection alone is not enough to prevent return of the disease in many patients. Adjuvant therapies (applied after initial treatment with the goal of suppressing secondary tumor formation) are often needed to improve survival.

Sunitinib and sorafenib are examples of adjuvant therapies known as kinase inhibitors. Kinases are proteins on or near the surface of cells; they help cancer grow and survive. Kinase inhibitors block the growth of kinases and associated blood vessels which nourish cancers. Sorafenib and sunitinib, which are taken in pill form on a daily basis, are thought to block different kinases.

Both drugs have been shown to be effective when kidney cancer has spread to other parts of the body. Could they also be effective in preventing recurrence of the disease?

"The current standard of care for these patients is close observation," Haas said. "Unfortunately, we found that the use of sunitinib or sorafenib in this setting did not reduce the incidence of recurrence as compared to placebo. Fortunately, the use of these drugs in this setting did not appear to make the outcome of patients receiving them any worse."

The findings closely mirror those of adjuvant trials in other tumors, such as breast and metastatic colorectal cancers, in which the benefits of bevacizumab in metastatic disease were not seen in the adjuvant setting.

This study, designed and conducted by ECOG-ACRIN, is the first and largest trial on the effectiveness of these two kinase inhibitors in patients whose kidney tumors have been completely removed and who are at high risk for recurrence. Haas said that there are other ongoing adjuvant trials investigating different lengths of therapy with sunitinib and sorafenib, as well as different kinase inhibitors. The results of these investigations are not yet available and could have different results than the Penn study.

"It is important to support these trials so we learn how to better treat kidney cancer in the adjuvant setting," she said.

In the early years of the trial, about a third of patients stopped treatment because they found the side effects, such as hypertension and fatigue, of the medications too hard to tolerate.

Patients in the study also contributed blood and urine samples as a part of their participation. Ongoing analyses of these samples may shed light on who might still benefit or not benefit from sunitinib and sorafenib in the treatment of kidney cancer in the adjuvant setting or point to other therapies that target specific pathways or tap into the immune system.

Haas and her colleagues collected the samples at the beginning of treatment and subsequent to recurrence of the cancer in patients who suffered a relapse—and continue to do so more than five years after the formal conclusion of the study.

"This will afford opportunities to uncover molecular clues and other information that could help explain why some patients had a recurrence of their cancer or a spreading elsewhere and others did not," Haas said.

There are also plans for a perioperative trial with an immune checkpoint inhibitor with this group of patients set to open in the near future.

ECOG-ACRIN Cancer Research Group is a membership-based scientific organization that focuses on cancer research involving adults who have or are at risk of developing cancer. It is comprised of nearly 1100 member institutions, including Penn Medicine.

Provided by University of Pennsylvania School of Medicine