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Targeted drug shows promise in rare advanced kidney cancer

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Some patients with a form of advanced kidney cancer that carries a poor prognosis benefited from an experimental drug targeted to an abnormal genetic pathway causing cancerous growth, according to research led by a Dana-Farber Cancer Institute scientist.

The drug, savolitinib, showed clinical activity in patients with metastatic papillary renal cell carcinoma (PRCC) whose tumors were driven by overactivity of the MET signaling pathway, but was not effective for patients whose tumors lacked the MET abnormality, said the investigators, led by Toni Choueiri, MD, director, Lank Center for Genitourinary Oncology, and director, Kidney Cancer Center, both of Dana-Farber.

These results from a single-arm, multicenter phase II clinical trial, reported in the *Journal of Clinical Oncology*, suggest that savolitinib holds promise as a personalized treatment for a subgroup of patients with metastatic papillary renal cell carcinoma, the researchers said.

In the US alone, about 6,400 cases of PRCC are expected to be diagnosed in 2017, compared to a total of 64,000 cases of kidney cancers. The majority of them are classified as clear cell renal cell cancers. Papillary renal cell carcinoma are non-clear cell kidney cancers. No good treatments exist for advanced or metastatic PRCC.

The current trial tested savolitinib, a potent and selective MET inhibitor, in 109 patients with locally advanced or metastatic PRCC. Of the 109

patients, 40 percent had tumors driven by MET, 42 percent had tumors that did not rely on MET, and MET status was unknown in 17 percent of patients.

When the results were analyzed, 18 percent of patients with MET-driven cancers had significant shrinkage of their tumors, and 50 percent had stable disease. By contrast, none of the patients with MET-independent tumors had shrinkage response, and only 24 percent had stable disease.

In addition, the length of time after treatment before the cancer began growing was significantly longer in the MET-driven tumor group - 6.2 months versus 1.4 months.

"These data support the hypothesis that savolitinib has antitumor activity in patients with MET-driven papillary renal cell carcinoma," the authors wrote. "Our study identified a defined molecular group and highlights the prevalence of MET-driven disease in this rare population of RCC patients."

Although some patients had their dosage of savolitinib reduced and two patients discontinued treatment because of side effects, the researchers said the drug was generally well-tolerated.

Provided by Dana-Farber Cancer Institute