2-drug combination appears safe and active in metastatic kidney cancer

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Fox Chase Cancer Center investigators report that a two-drug blockade of mTOR signaling appears safe in metastatic kidney cancer in a phase I trial. Early data suggests that a combination of temsirolimus and bryostatin may be active in patients with rare forms of renal cell cancer, which are less likely to respond to other targeted therapies.

Elizabeth Plimack, M.D., M.S., a medical oncologist and attending physician at Fox Chase will report the trial results on Sunday, May 31 at the annual meeting of the American Society of Clinical Oncology.

"We have certainly seen sustained responses with this combination which are encouraging," Plimack says.

One of the patients with an extended response has papillary renal cell cancer, which is a rare form of the disease that does not respond well to standard therapies. "Patients with non-clear cell renal cell cancer, including papillary renal cancer, don't respond as well to tyrosine kinase inhibitors, such as sunitinib and sorafenib, as patients with clear cell renal cell. So there is an unmet need for therapy for these patients. We've seen that this combination may be active to some degree for them."

mTOR signaling promotes tumor cell proliferation and blood vessel development. Temsirolimus (Torisel), blocks signaling through one portion of the mTOR signaling complex, called TORC1, and slows tumor progression in patients with advanced kidney cancer. However, a

second portion of the complex, called TORC2, is unaffected by temsirolimus and continues to promote cell proliferation. Therefore, Plimack and colleagues suspect that blocking TORC2 signaling activity could improve patient outcomes. Bryostatin blocks a downstream effector of TORC2, called protein kinase C.

Plimack and colleagues designed the phase I trial to test the safety of the bryostatin-temsirolimus combination. Twenty-five patients enrolled in the trial, including 20 patients with renal cell carcinoma. The phase I trial tested a combination of 20 micrograms/m2 bryostatin weekly plus one of the following temsirolimus doses, 10, 15, 25, or 37.5 mg, every 28 days.

The combination appears to be well tolerated in renal cell patients. Two patients developed dose limiting toxicities (one with renal toxicity and one with neutropenia) at the highest temsirolimus dose. Enrollment is now continuing with patients receiving 25 mg temsirolimus. (Two of the non-renal cell cancer patients developed dose-limiting toxicities early in the trial, after which point the investigators limited enrollment to patients who had not received prior chemotherapy.)

Early responses in renal cell cancer patients are promising, according to Plimack. Three patients have had durable partial responses to therapy. Two of those individuals are off therapy and have partial responses continuing at 3+ years and 12+ months, and a third patient continues on therapy with a partial response extending beyond 22 months.

Enrollment in the trial is on-going and complete data will be provided at the meeting.

Source: Fox Chase Cancer Center (news : web)