Targeted investigational therapy shows early promise against multiple cancer types

April 9 2014

The investigational, oral drug BGJ398, which blocks the activity of a family of proteins called fibroblast growth factor receptors (FGFRs), showed promising anticancer activity in patients with various types of cancer driven by FGFR genetic alterations, according to the results of a phase I clinical trial presented here at the AACR Annual Meeting 2014, April 5-9.

Genetic alterations in FGFRs play a role in driving tumor growth for a subset of patients with a variety of cancers, including squamous cell lung carcinoma and urothelial bladder cancer," said Lecia V. Sequist, M.D., M.P.H., associate professor of medicine at Harvard Medical School and Massachusetts General Hospital in Boston. "The primary purpose of this phase I, first-in-human clinical trial of BGJ398 was to look at how the drug is tolerated by patients. However, we specifically enrolled only patients with FGFR genetic alterations in their tumors because we predicted these patients would have the greatest chance of benefiting from the drug.

"We were very excited to see that the drug had activity against several different types of cancer, including bladder cancer, for which we have very few treatment options," added Sequist. "By showing that patients with FGFR genetic abnormalities can respond to an FGFR inhibitor, we have clearly demonstrated the value of a personalized approach to cancer therapy with a targeted agent."

Sequist and colleagues enrolled in their trial 107 patients with a tumor

shown to have an FGFR genetic alteration by central or local prescreening. Most patients had squamous cell lung carcinoma or breast cancer, but patients with a variety of other cancers, including cholangiocarcinoma and urothelial cell/bladder cancer, also participated.

Forty-three patients were treated in the dose escalation phase of the trial. In the expansion phase of the trial there were three groups, or arms. In the first were 18 patients with FGFR1-amplified squamous cell lung carcinoma who received BGJ398 daily; in the second and third were 21 and 25 patients with other cancers harboring FGFR genetic alterations who received the drug daily for four weeks and daily for three weeks followed by a week off, respectively.

The researchers saw anticancer activity, as assessed by tumor shrinkage after treatment, in patients who participated in the dose escalation phase and received 100 mg or more of the drug per day, and among patients in all three expansion arms. They saw tumor shrinkage in patients with various types of cancer, including four of five patients with FGFR3-mutated urothelial cell cancer. For two of these patients, tumor shrinkage was more than 30 percent, which means they had an "official" partial response. One partial response in a patient with FGFR1-amplified squamous cell lung carcinoma has previously been reported. Anticancer activity was also seen for other patients with squamous cell lung carcinoma, squamous cell head and neck cancer, breast cancer, and cholangiocarcinoma.

The most common side effect was elevated levels of the blood mineral phosphorus. According to Sequist, in this study and future studies, patients being treated with FGFR inhibitors will also need to take phosphate-lowering medications to help balance this.

"A number of phase II clinical trials are ongoing or planned, including a study in patients with the most lethal form of brain cancer, glioblastoma

multiforme," said Sequist. "Work is ongoing to further identify what specific FGFR genetic alterations correlate with response to BGJ398. In this regard, given our results with the urothelial cell/bladder cancer patients, we are actively screening these patients to look for FGFR3 genetic alterations in order to try to give them the opportunity to be treated with BGJ398."

Provided by American Association for Cancer Research