ICU
MANAGEMENT & PRACTICE

Vitamin K With Sorafenib Showed Anti-tumor Effects In Pancreas Cancer, Hepatocellular Carcinoma

A combination of sorafenib and vitamin K had an effect in vitro on both human pancreas cancer and hepatocellular carcinoma, according to researchers from the Kimmel Cancer Center at Jefferson. Data from the two studies were presented at the AACR 100th Annual Meeting 2009 in Denver.

Vitamin K1 or vitamin K2, plus sorafenib (Nexavar) each have shown activity against the growth of human cancer cells by inhibiting the extracellular signal-regulated kinase (ERK) pathway according to Brian Carr, M.D., Ph.D., a professor of Medical Oncology at the Jefferson Medical College of Thomas Jefferson University. ERK plays a major role in cell growth of cancers.

Although sorafenib has demonstrated success at extending survival in patients with hepatocellular carcinoma (HCC, or primary liver cancer), hand-foot syndrome is a common adverse effect that affects approximately 20 percent of patients who receive the drug. It typically manifests as painful sores on the soles of patients' feet that can prevent the patients from walking, Dr. Carr said. Profound tiredness and weight loss is also seen in at least 30 percent of patients.

In the pancreas cancer study, Dr. Carr and his colleagues tested each K vitamin in combination with sorafenib in pancreatic cell lines. Each combination inhibited cell growth, induced cell death and decreased the expression of ERK. They found that when combining vitamin K and sorafenib, the sorafenib dose required for inhibiting cancer cell growth decreased by more than 50 percent. This dose was ineffective when used alone.

"So few agents have activity against pancreas cancer," Dr. Carr said. "One of the attractions of the combination of sorafenib and vitamin K is that both of these agents are already approved for human use. K vitamins also have no known adult human toxicities, and appear to enhance the effects of sorafenib, thus requiring lower, less-toxic doses."

In the second study, vitamin K1 also enhanced the effects of sorafenib in HCC. Sorafenib is FDA-approved for the treatment of HCC, which typically arises on a cirrhotic liver, which tolerates conventional chemotherapy poorly. The researchers previously had shown that vitamin K alone is a weak inhibitor of HCC growth. In this study, they found that the combination inhibits the growth of HCC, induces cell death and decreases the expression of ERK.

"Many patients need to discontinue treatment with sorafenib because of the debilitating side effects," Dr. Carr said. "If we could lower the dose, more patients would be able to complete their treatment."

These data also pave the way for potential studies to evaluate the combination of sorafenib and vitamin K as an HCC prevention strategy in patients who are at greater risk for developing the disease. This population includes patients with cirrhosis or patients who have previously had surgery for HCC. According to Dr. Carr, the recurrence rate for HCC after surgery is 40 percent.

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