MedicalXpress

Researchers report first success of targeted therapy in most common non-small cell lung cancer

November 28 2012

A new study by an international team of investigators led by Dana-Farber Cancer Institute scientists is the first to demonstrate that chemotherapy and a new, targeted therapy work better in combination than chemotherapy alone in treating patients with the most common genetic subtype of lung cancer.

Published online today in *The* Lancet Oncology, the combination of chemotherapy and the targeted drug selumetinib was more effective than chemotherapy alone in a clinical trial involving patients with a form of non-small cell lung cancer (NSCLC) that carries a mutation in the gene KRAS – a variety that represents about 20 percent of all NSCLC cases. Previously, no targeted agent, either alone or in combination with another drug, had proven beneficial in a trial involving patients with this type of NSCLC.

The 87 patients who participated in the new, phase II trial – conducted at 67 sites around the world – had advanced, KRAS-mutant NSCLC that had failed initial chemotherapy. The participants were randomly assigned to receive either selumetinib and the chemotherapy agent docetaxel or docetaxel alone.

Investigators found that while 37 percent of the patients in the selumetinib group experienced some shrinkage of their tumor, none of the patients in the docetaxel-only group did. Of particular significance,

patients receiving selumetinib lived a median of 5.3 months before their cancer began to worsen, compared to 2.1 months for those receiving chemotherapy alone. (Patients in the selumetinib group also survived longer, on average, than those in the docetaxel group – 9.4 months compared to 5.2 months – but the improvement was not considered statistically significant.)

"Our findings suggest that selumetinib and docetaxel work synergistically – each enhancing the effect of the other," says the study's lead author, Pasi A. Janne, MD, PhD, of Dana-Farber. "This opens the possibility that there may finally be a therapeutic strategy using a targeted therapy which could be clinically effective in this population of KRAS-mutant lung cancer patients."

Some side effects, including neutropenia (a white blood cell deficiency), neuropenia plus fever, shortness of breath, and loss of strength, were more common in the selumetinib group than the other.

Researchers and physicians will need to work on ways of managing these problems with patients, Jänne said.

NSCLC tumors with KRAS mutations are more common in current and former smokers than in those who have never smoked, and occur at a higher rate in Caucasians than in others. The study findings are especially noteworthy because mutated KRAS – regardless of the type of tumor it appears in – has been one of the most difficult genes to block with targeted therapies.

Selumetinib circumvents that problem by targeting not KRAS itself, but one of the gene's co-conspirators, a protein called MEK that is indirectly activated by KRAS.

"The opportunity now is to validate this approach in further clinical trials

so it can be developed into a real therapy for patients," Jänne remarks. "Given that KRAS mutations are common in other cancers (found in 90 percent of pancreatic cancers and 40 percent of colon cancers), our findings may be useful in developing therapies for patients with these cancers as well."

Provided by Dana-Farber Cancer Institute