Targeted therapy boosts lung cancer outcomes

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–Thousands of patients with an advanced form of lung cancer that carries a specific dysfunctional gene are likely to fare better if treated with a targeted therapy than with traditional chemotherapy, report Dana-Farber Cancer Institute researchers and a team of international collaborators.

In a trial involving patients with non-small cell lung cancer (NSCLC) whose tumor cells harbored an abnormal ALK gene, those who received the oral drug crizotinib, which acts directly on ALK, went a median time of 7.7 months before their disease began to worsen, compared to 3 months for patients who received traditional chemotherapy. Patients treated with crizotinib also had a better quality of life than those treated with standard chemotherapy. The findings will be released as an advanced online publication by the *New England Journal of Medicine* on June 1.

"This study demonstrates the value of testing lung cancer tissue for an ALK rearrangement, and it underscores the potential of cancer genomics to target cancer treatments to each patient," says the study's senior author, Pasi A. Jänne, MD, PhD, who is the director of the Lowe Center for Thoracic Oncology of Dana-Farber. "ALK now becomes the second abnormal gene that we are able to successfully target in lung cancer with drugs other than chemotherapy." Lung cancers with the first such gene, EGFR, are now commonly treated with EGFR inhibitors before chemotherapy.

The lead author of the study is Alice Shaw, MD, PhD, of Massachusetts General Hospital.

NSCLC is the most common form of lung cancer, striking nearly 200,000 people in the U.S. each year. Although abnormal ALK is found in only about 5 percent of NSCLC cases, that translates into more than 5,000 new patients annually who could potentially benefit from crizotinib therapy, the study authors state.

The phase 3 trial described in the paper involved 347 patients with advanced or metastatic NSCLC who had already been treated with standard chemotherapy. The most common side effects associated with crizotinib therapy – visual disorders, gastrointestinal problems, elevated liver enzymes, and leg swelling – were generally mild, Jänne said, and are markedly different than the fatigue and hair loss associated with chemotherapy.

The abnormality in ALK that arises in NSCLC is not, strictly speaking, a mutation (a change in the sequence of DNA within a gene). Rather, it results from a chromosomal rearrangement, in which the structure of a chromosome – the scaffolding of genetic material – is altered.

Crizotinib is a drug agent that takes aim at key enzymes within cells called kinases, which are often abnormal in cancer. Originally designed to block a kinase called MET, it was later discovered to target ALK as well. At the time, it wasn't known that ALK was sometimes abnormal in lung cancer. The discovery that it is abnormal in a small percentage of NSCLCs led to its testing against the disease.

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