People with specific kind of lung cancer respond to new targeted treatment

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A study in the *New England Journal of Medicine* shows more than half of patients with a specific kind of lung cancer are responding positively to a treatment that targets the gene that drives their cancer.

The study shows 57 percent of patients with ALK-positive advanced non-small cell lung cancer responded partially or completely to a tablet called crizotinib, an investigational anaplastic lymphoma kinase (ALK) inhibitor. In some cases, the cancer becomes undetectable in body scans. The data is published in the October 28 issue of the New England Journal of Medicine.

"This study really supports the idea that we should always try to identify the patients that could benefit from a specific treatment in advance. By looking at lung cancer at the molecular level, we were able to find the patients most likely to respond to the ALK inhibitor and put them in this trial," said D. Ross Camidge, MD, PhD, one the of the study's authors, director of the lung cancer clinical program at University of Colorado Hospital (UCH) and the University of Colorado Cancer Center (UCCC).

"At the University of Colorado Hospital, we look after one of the largest groups of ALK positive lung cancer patients in the world. About one in 20 lung cancer patients are ALK positive. Most feel better within days of beginning the drug in the trial and many have returned to active lifestyles with their cancer under excellent control." said Camidge.

There were initially 82 ALK-positive lung cancer patients in the trial of

the ALK inhibitor. ALK is believed to be a key driver of tumor development in some cancers.

Updated results from the study were presented earlier this month at the 35th Congress of the European Society for Medical Oncology (ESMO) in Milan, Italy, reporting on a total of 113 patients and the impressive activity of the drug in these patients remained consistently high. The preliminary median progression-free survival (PFS), the time it takes for the cancer to first start to grow again, was 9.2 months.

"Initially the cancer melts away, but it's still there. And at some point, it usually figures out a way to get around this particular drug. We need to keep looking for new developments so that when this happens, we can supplement or replace the crizotinib with other treatments to help keep the cancer under long-term control," said Camidge.

At the very least, Camidge said it is crucial for anyone diagnosed with lung cancer to get their tumor tested. Several commercially available tests are available but the definitive test that qualifies for entry into the study is only conducted in those centers with the trial. The University of Colorado helped to develop these tests and many others for taking one disease - lung cancer - and revealing that it is, in fact, several different diseases at the molecular level. Each one of the diseases may need a different treatment.

Study Results Published in the *New England Journal of Medicine*

In the Part 2 expansion cohort study which included 82 patients with ALK-positive advanced NSCLC, 57 percent (n=47)(95% CI 46%, 68%) of patients treated with crizotinib (PF-02341066) at a dose of 250 mg twice daily, had either a complete or partial response to treatment. An additional 33 percent (n=27) met criteria for stable disease, including five unconfirmed partial responses. At eight weeks, the disease control

rate (complete response (n=1) + partial response (n=46) + stable disease (n=24)) was 87 percent (n=71). Three patients with stable disease were not included in the disease control rate because their evaluation for response was outside a pre-specified timeframe.

At the time of the analysis, 77 percent of patients (n=63) continued to receive treatment with crizotinib (PF-02341066). The median duration of treatment was 6.4 months, and follow-up is ongoing. As such, the estimated probability of being progression-free at six months is 72 percent (95% CI: 61%, 83%).

Overall, crizotinib (PF-02341066) was generally well tolerated. The most commonly reported all-grade adverse events included nausea (n=44), diarrhea (n=39), vomiting (n=36), and mild visual disturbances (n=34). Grade 3 ALT (alanine aminotransferase) and AST (aspartate aminotransferase) elevations occurred in four patients. One patient experienced a Grade 4 ALT and one patient discontinued treatment due to Grade 3 ALT increases. Tumors in the analysis were primarily of adenocarcinoma histology, and patients tended to be young, and were never or former light smokers. Ninety-three percent of patients (n=76) had received at least one prior therapy and five patients were treated in the first-line setting.This Part 2 expansion cohort study of patients with ALK-positive advanced NSCLC, independent of the number of previous chemotherapies, followed the completion of the dose-escalation study which enrolled 37 advanced cancer patients with various tumors, including NSCLC, colorectal, pancreatic and inflammatory myofibroblastic tumor (IMT) tumors.

These data were previously presented at the 2010 American Society of Clinical Oncology Annual Meeting.

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