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Survival over single-line treatment improved with use of combo drug cancer therapy

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A combination therapy for treating cancer discovered at the University of Colorado Cancer Center showed improved survival rates in patients with advanced non-small cell lung cancer (NSCLC), according to results from a double-blind, placebo-controlled phase 2 trial run by Syndax Pharmaceuticals.

The phase 2 results show that the combination of entinostat (Syndax's SNDX-275) and erlotinib was more effective in treating NSCLC in patients with elevated levels of the molecular cancer marker E-cadherin than using erlotinib alone. University of Colorado Cancer Center researchers, who are faculty at the University of Colorado School of Medicine, were the first to identify elevated E-cadherin as a targetable cancer marker, the first to develop the biomarker tumor testing process for elevated E-cadherin and the first to test the combined therapy.

About 40 percent of NSCLC patients have elevated E-cadherin levels, making this a significant advance towards highly personalized treatment for lung cancer patients. Entinostat controls expression of genes that can cause resistance to conventional cancer therapies like erlotinib.

"The outcome of patients with advanced lung cancer has been disappointing historically but the identification of new molecular features and new therapies directed at these molecular features has markedly improved outcome for some patients," said Paul Bunn, MD, professor of medical oncology at the CU medical school and principal investigator of the University of Colorado Cancer Center's Specialized

Program of Research Excellence in Lung Cancer, funded by the National Cancer Institute.

“Unfortunately, some of the molecular changes are quite rare,” said Bunn. “A more common molecular change is the high expression of epithelial markers such as Ecadherin. HDAC inhibitors such as etinostat can increase the expression of epithelial markers and can delay the development of resistance to EGFR inhibitors such as erlotinib. In this study, the combination of erlotinib and the HDAC inhibitor etinostat lead to a small but not statistically significant improvement in survival in unselected patients but a large and statistically significant improvement in survival in patients with high expression of Ecadherin (9.4 months vs.5.4 months). While extremely promising, these results will need to be confirmed in a larger randomized phase III trial.”

"Using a biomarker to select patients based on the tumor biology can improve patient outcomes versus treating an unselected patient population," said University of Colorado Cancer Center researcher Fred Hirsch, MD, PhD, professor of medical oncology at the CU medical school.

Data from the phase 2 trial, led by Robert Jotte, MD, PhD, of Denver’s Rocky Mountain Cancer Center, was presented recently at the ASTRO 2010 Chicago Multidisciplinary Symposium in Thoracic Oncology, co-sponsored by the American Society for Radiation Oncology, the American Society of Clinical Oncology, the International Association for the Study of Lung Cancer and The University of Chicago.

“The data presented suggest that NSCLC patients with elevated E-cadherin levels can do better when treated with entinostat and erlotinib,” said Joanna Horobin, MD, president and chief executive officer of Syndax, the company that holds worldwide rights to entinostat.

Syndax holds rights to the CU intellectual property related to this type of combination therapy which includes the use of E-cadherin to predict responsiveness to the therapy.

“Syndax has been a model commercial partner for the University, and we are both encouraged and excited by the Phase 2 results,” said David Poticha, senior licensing manager at the CU Technology Transfer Office.

More information: For more information regarding the presentation please visit www.thoracicsymposium.org/.

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