Online screening for rare lung cancer subtypes opens door to new kind of clinical trial

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Ross Camidge, M.D., Ph.D., director of the thoracic oncology clinical program at the CU Cancer Center is principal investigator of clinical trial testing ponatinib against FGFR+ lung cancer. Credit: University of Colorado Cancer Center

In the previous few years, several breakthrough treatments have become available for key subtypes of lung cancer. Patients who may benefit from these treatments can be pre-identified by looking for defined genetic abnormalities in their cancer. For example, patients whose lung cancer is driven by rearrangement of the gene ALK derive significant benefit from the drug crizotinib, which targets this abnormality. Many ongoing clinical trials are now attempting to replicate this success by matching different drugs with specific subtypes of the disease based on the presence of such "predictive biomarkers." However, testing these new drugs in clinical trials requires finding and enrolling patients with what may be very rare molecular subtypes of a disease – one of the challenges is discovering enough needles in enough haystacks to prove the effectiveness of each biomarker-drug pairing.

The University of Colorado Cancer Center is now taking a novel approach to this problem, reaching out via the internet to expand the pool of patients potentially eligible for just such a biomarker-preselected clinical trial. After completing the interactive online screening questions, eligible patients with advanced lung cancer will be consented via the phone to permit a pre-existing biopsy sample of their lung cancer tissue to be shipped to the CU Cancer Center for trial-specific molecular testing. The testing is designed to identify patients who may have lung cancers driven by alterations in the gene FGFR1. Patients whose tumors turn out to be FGFR1-positive and meet the other trial screening criteria will then be offered treatment for their cancer within a clinical trial at CU Cancer Center using the experimental FGFR1 inhibitor drug ponatinib. Ponatinib is already licensed for treating certain blood cancers, but work by CU scientists in laboratory models suggest it may also be a potent agent in some specific molecular subtypes of lung cancer driven by, among other things, changes in the FGFR1 gene.

"FGFR1 has already been explored by the pharmaceutical industry, with rather limited success, but those approaches used a very different way of

looking to see if FGFR1 was driving the lung cancer," says Ross Camidge, MD, PhD, director of the thoracic oncology clinical program at the CU Cancer Center and the trial's principal investigator. "Based on some really innovative work coming out of our own Specialized Program of Excellence in Lung Cancer, the tests we are employing in this trial seem to define a completely separate subtype of lung cancer – one that has really not been explored before. Now the challenge is in finding enough people whose cancers are positive for our biomarkers to prove whether the markers will predict for clinical benefit from ponatinib."

Having built the infrastructure to allow nationwide molecular prescreening for the trial, Camidge's team plans to also use internet awareness to speed accrual into their trial.

"We know that the vast majority of the U.S. population now routinely uses the internet to find out about medical conditions, so we thought we'd get Dr. Google to help us out," says Camidge. "Several very high profile internet resources for lung cancer patients, including the Bonnie J. Addario Lung Cancer Foundation (BJALCF) and the Global Resource for Advancing Cancer Education (GRACE) have helped us craft this trial and we are very grateful for their commitment to increase awareness about the opportunity it presents for lung cancer patients who might benefit from the molecular prescreening."

Indeed, Dr Jack West, the CEO of GRACE, co-wrote a position paperwith Camidge in the *Journal of Thoracic Oncology* in 2012 titled "Have Mutation, Will Travel" to highlight the pressing need to transform the way clinical trials are conducted in the new era of molecular diversity.

"While Big Pharma sometimes spends millions of dollars to open biomarker-selected trials at hundreds of different locations to find enough patients, the kind of innovative approaches that are homegrown

in university settings will never have the resource to do that," said Dr West. "Regardless of whether the FGFR1-ponatinib pairing works or not, what the Colorado team is trying to do could really change the future of clinical cancer research for the better. Patients are increasingly becoming empowered about their own cancer care. Anything we at GRACE can do to get the word out about the Colorado approach will be a very good thing."

Bonnie Addario, chair and founder of the BJALCF and a ten-year lung cancer survivor herself, is similarly enthusiastic. "If we are going to change the survival rates for lung cancer, we have to stop treating everyone the same. We have to do things differently, and if Dr. Camidge's approach can bring a little bit of Colorado's expertise into easy reach of anyone with a computer, then this is a new way of accelerating the process and much more convenient for the patient. We will do all we can to assist in getting patients involved in this exciting new approach," Addario says.

Over the next 3-5 years the Colorado team plans to screen up to 700 lung cancer patients and optimize the biomarker signatures for predicting benefit from ponatinib over time, tweaking the criteria as they go along based on the emerging results in each group of treated patients.

"Clinical research is very expensive and sources of support for this kind of clinical research, as for everything else, are rather limited," says Camidge. However, Camidge's novel approach has already allowed him to secure several hundreds of thousands of dollars in support from sponsors including the manufacturer of ponatinib, Ariad, from the CU Cancer Center and from the CU Lung Cancer Specialized Program of Excellence in Lung Cancer.

"However, if this trial takes off, that's probably only about half of what we'll need. That's why we've taken to the internet to crowd-source trial

accrual through the Consano philanthropy website. It's amazing—the internet is giving us new opportunities at every turn. I am very optimistic; although we are having to do this on a very limited budget, I know from experience that we can produce major breakthroughs even from a small study if the approach is right," Camidge says.

More information: Search "UC Denver ponatinib" to visit the trial enrollment website, or perform similar searches on the Consano crowd sourcing website, or at ClinicalTrials.gov to learn more about the study.

Provided by University of Colorado Denver