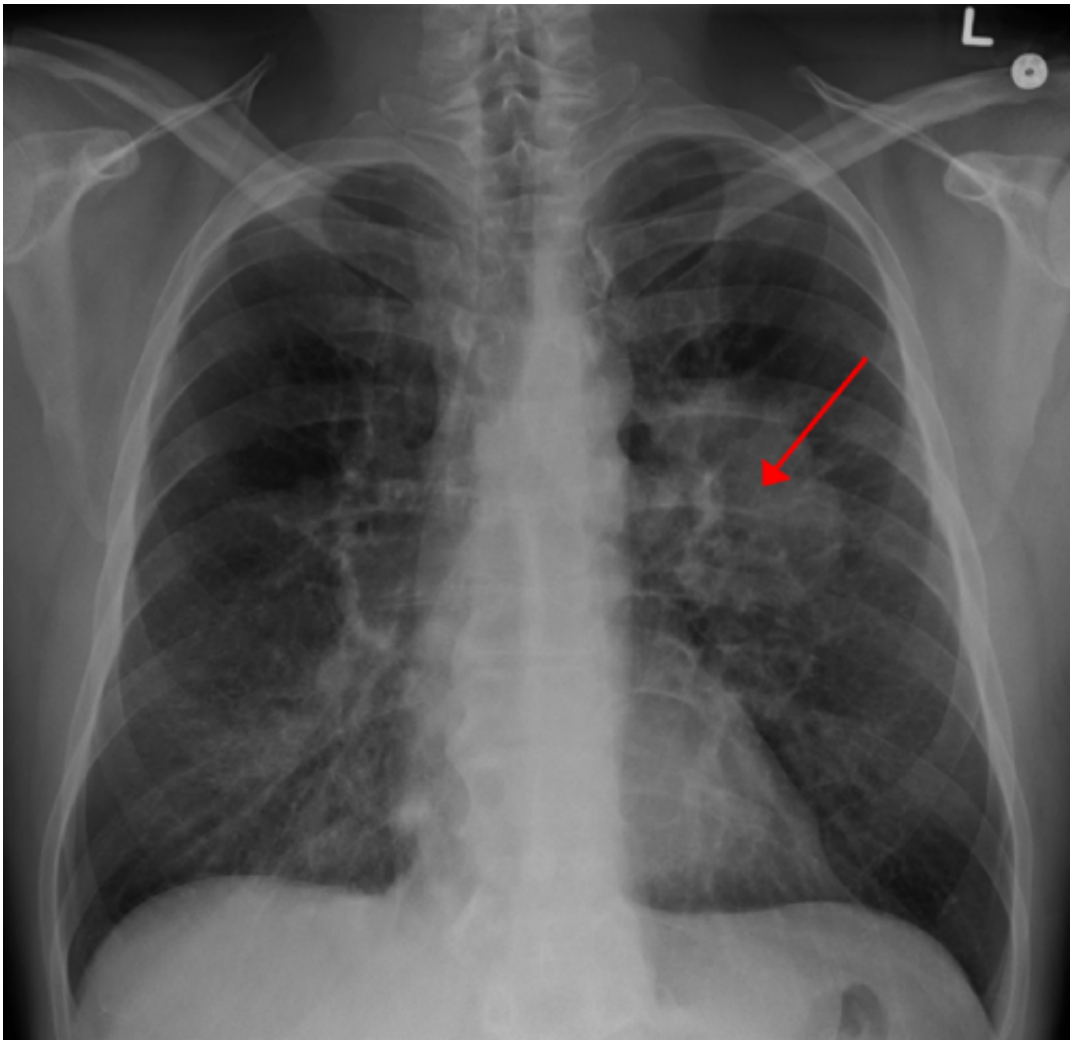
Genomic tumor testing to match lung cancer patients with targeted drugs transforms care

May 20 2014



Lung CA seen on CXR. Credit: CC BY-SA 4.0 James Heilman, MD/Wikipedia

New data from a study led by Memorial Sloan Kettering physicians that used targeted therapy for patients with the most common type of lung cancer has helped transform treatment for the disease.

The Lung Cancer Mutation Consortium (LCMC), composed of a group of 14 US hospitals, incorporated tumor genotyping into therapeutic decision-making for patients with lung adenocarcinomas. An oncogenic driver was detected in 64 percent of tumors from patients in this study. Oncogenes, when activated by genetic mutations, can turn normal cells cancerous. Data from this study that will be published in the May 20 issue of the *Journal of the American Medical Association* shows that survival may be improved when drugs matched to the oncogenic drivers identified through this program are given to patients.

"This has transformed the way we treat people with lung cancers," said lead co-author Mark G. Kris, MD, the Ruane Chair in Thoracic Oncology at Memorial Sloan Kettering. "It used to be that when lung cancers were diagnosed solely by a visual microscopic examination of tumor tissues by a pathologist, every patient received the same intravenous chemotherapy. But now, we are personalizing the care of these individuals by finding the genetic alterations in the tumor tissues that drive their cancers and giving medicines that specifically counteract the cancerous effects of those genes."

Dr. Kris and colleagues used multiplex genetic testing to analyze DNA from tumor tissues and perform other techniques to detect the presence of ten driver oncogenes in more than 1,000 patients from 14 different hospitals across the United States. Patients with oncogenic drivers who received targeted drug treatment had a median survival of about 3.5 years; patients with oncogenic drivers who did not receive targeted therapies had a median survival of about 2.4 years; and patients with no identified oncogenic driver had a median survival of 2.1 years.

Although individuals with oncogenic drivers who received targeted drug treatment lived longer, randomized clinical trials are required to determine if selecting targeted therapy based on oncogenic drivers improves survival.

Once the driver oncogenes were identified in a patient's tumor specimen, the information was given to their doctors to be used in selecting treatments.

The study included patients with stage IV or recurrent adenocarcinomas of the lung. Tumors from 1,007 patients were tested for at least one gene; 733 patients had tumors fully genotyped and were tested for ten genes. Among the latter group, oncogenic drivers were identified in 64 percent of the tumor specimens. Doctors were able to recommend a targeted drug therapy from either the pharmacy or a clinical trial in 28 percent of those cases.

"When we find these specific genetic changes, the doctor can choose drugs and clinical trials specifically targeting those oncogenic drivers. When that happens, the chance of shrinkage is much higher than with standard chemotherapies. The side effects are much less because the cancer cells are much more dependent on these oncogenes than normal cells," said Dr. Kris.

Memorial Sloan Kettering has been a leader in using cancer genetic testing and genomics to guide the care of individual patients with lung cancers since 2004, when MSK pathologists devised routine tests for oncogenic drivers. This effort followed the 2003 discovery of mutations in the epidermal growth factor receptor (EGFR) at Memorial Sloan Kettering and two Boston hospitals.

"This study showed that we can routinely and simultaneously test for the most important genetic changes in the tumors of patients with lung

cancers," said Marc Ladanyi, MD, Memorial Sloan Kettering's Chief of Molecular Diagnostics and co-investigator on the study. "This information can guide the selection of targeted therapies to treat lung cancer patients because a key finding of the study suggested better outcomes for patients whose tumors had oncogenic drivers and who were given the appropriate targeted treatment. Our testing capabilities have grown tremendously in the last decade. Our latest multiplex genetic testing assay, MSK-IMPACT, has expanded well beyond lung cancers to use next-generation sequencing to routinely assay 341 cancer-related genes in all types of solid cancers."

Adenocarcinomas are diagnosed in 130,000 patients in the United States and 1 million people worldwide each year.

More information: Paper: doi:10.1001/jama.2014.3741
Editorial: doi:10.1001/jama.2014.3742

Provided by Memorial Sloan-Kettering Cancer Center