



What to Know: The CAP/ IASLC/AMP Guideline on Test Selection of *EGFR* Mutation and *ALK* Rearrangement in Lung Cancer

Introduction:

The new frontier of precision medicine offers patients the opportunity for molecular testing, leading to optimal targeted, individualized treatment based on their genetic profile. To help pathologists and oncologists provide the best possible patient care, the College of American Pathologists (CAP), the International Association for the Study of Lung Cancer (IASLC), and the Association for Molecular Pathology (AMP) have developed an evidence-based guideline to provide recommendations for the test selection for *EGFR* mutation and *ALK* rearrangement in lung cancer. The implementation of the guideline will identify patients who could benefit more from new targeted drugs than from conventional chemotherapy, while experiencing fewer side effects. Below is a link to the guideline:

[Molecular Testing Guideline for the Selection of Lung Cancer Patients for *EGFR* and *ALK* Tyrosine Kinase Inhibitors](#)

Key Points:

- Physicians should order *EGFR* mutation and *ALK* rearrangement testing at the time of diagnosis for patients with advanced stage lung adenocarcinoma, regardless of their clinical history.
- In the United States, up to 20 percent of patients with lung adenocarcinoma, the most common type of lung cancer, will test positive for one of the two biomarkers, *EGFR* and *ALK*, and will benefit from targeted drugs matched to these biomarkers.
- Patients with advanced stage lung adenocarcinoma should ask to be tested for *EGFR* and *ALK* and should also ask if their testing is being performed in an accredited laboratory.
- The molecular changes, if present, are only in the cancer cells, not in normal cells and are not inherited. Therefore, there are no concerns for their family members.
- The molecular testing will identify patients for oral therapy. Standard therapies will be used as well.

Background

Below is additional information about *EGFR* mutation and *ALK* rearrangement and targeted therapies:

***EGFR* – Epidermal growth factor receptor**

The epidermal growth factor receptor (*EGFR*) is a normal gene that causes cells to divide when necessary to replace aging or injured cells in our bodies. Ordinarily it is only active

when cells need replacement. When cell replacement is required, surrounding cells produce and release a molecule called the epidermal growth factor (EGF), which binds and activates a specific receptor molecule (EGFR). When this happens, the EGFR then activates a series of other proteins in the cell to initiate growth and cell division, after which no more EGF is produced and the receptor becomes inactive. In cancer cells, however, the mutation causes the receptor to be constantly active even without any EGF present.

Mutations that lead to EGFR over-activity have been associated with lung cancer. New oral drugs directly inactivate the EGFR. *EGFR*-positive patients have shown a 70 percent response rate to treatment, which exceeds chemotherapy responses, lasting longer and with less toxicity.

***ALK* Rearrangement**

Anaplastic lymphoma kinase (*ALK*) is a similar gene that also causes cell division, but is not normally active in cells in the lungs. A genetic change called a rearrangement causes the *ALK* gene to break and then attach to another gene called *EML4*, which causes uncontrolled activation and cell division.

Rearrangements of genetic material involving the *ALK* gene increase the risk of cancer, including lung cancer. Standard tests can be used to detect patients with an *ALK* gene fusion. For those patients, an oral targeted therapy has a response rate of about 60 percent, which is higher than the response rate to chemotherapy, and is less toxic.

Recommendations

To ensure a uniform approach to the molecular testing of lung cancer, the CAP/IASLC/AMP guideline, "Molecular Testing Guideline for the Selection of Lung Cancer Patients for EGFR and ALK Tyrosine Kinase Inhibitors," recommends the following:

- All patients with advanced stage lung adenocarcinoma should be tested for *EGFR* and *ALK* abnormalities that would qualify them for EGFR and ALK inhibitor therapy—regardless of their clinical history.

The guideline also provides recommendations on how *EGFR* and *ALK* testing should be performed and if other genes should be routinely testing in lung cancer.

What This Means for Patients

Similar to the testing done in breast cancer, matching a cancer patient's molecular profile with the appropriate targeted therapy provides individualized treatment options that could improve quality of life and prolong it. In addition, new targeted therapies, in the form of a pill, have fewer side effects associated with them than conventional chemotherapy. For a man or woman battling lung cancer, the promise of more time with their loved ones and improved quality of life is priceless. Patients with advanced stage lung cancer are encouraged to speak with their physicians about receiving testing *EGFR* mutation and *ALK* rearrangement.

Role of the Pathologists in Determining *EGFR* and *ALK* Status

Pathologists, physicians who specialize in diagnostic medicine, identify tumor types and biomarkers through molecular testing of a patient's tumor. As experts in laboratory medicine, pathologists select the right test, at the right time, for the right patient and work collaboratively with a patient's oncologist to guide targeted therapies.

Questions to Ask Your Doctor

To learn more about testing for molecular biomarkers, *EGFR* and *ALK*, consider asking your doctor the following questions:

- Should I be tested for the two molecular biomarkers, *EGFR* mutation and *ALK* rearrangement?
- What were the results of my molecular tests?
- What targeted therapies are available to me?
- Is the laboratory performing my testing an accredited laboratory?

Publication:

The guideline was published on April 3, 2013, in the *Archives of Pathology & Laboratory Medicine*, *Journal of Thoracic Oncology*, and [The Journal for Molecular Diagnostics](#).

About CAP

- The [College of American Pathologists](#) (CAP) is a medical society with more than 18,000 physician members who specialize in diagnosing disease and it is the worldwide leader in laboratory quality assurance, celebrating more than 50 years as the gold standard in laboratory accreditation. The CAP is the world's largest organization composed exclusively of board-certified pathologists. The CAP advocates accountable, high-quality, and cost-effective patient care.

About IASLC

- The International [Association for the Study of Lung Cancer](#) (IASLC) is the only global organization dedicated to the study of lung cancer. Founded in 1974, the association's membership includes more than 3,500 lung cancer specialists in 80 countries.

About AMP

- The [Association for Molecular Pathology](#) (AMP) is an international medical professional association dedicated to the advancement, practice, and science of clinical molecular laboratory medicine and translational research based on the applications of molecular biology, genetics, and genomics.