



What to Know: The CAP/ IASLC/AMP Guideline on Test Selection for *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% 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 patients' 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% 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%, 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 tested 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?

Helpful Links:

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

To find a CAP-accredited laboratory in your community, visit the College's [Accreditation Laboratory Directory](#).

About CAP

As the leading organization for board-certified pathologists, the College of American Pathologists (CAP) serves patients, pathologists, and the public by fostering and advocating excellence in the practice of pathology and laboratory medicine worldwide. With more than 18,000 physician members, the CAP has led as the gold standard in laboratory accreditation for 50 years with more than 7,300 CAP-accredited laboratories in 50 countries. Find more information about the CAP at cap.org.

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.