

Lung Cancer Focused Panel Tests via Circulating Tumor DNA (ctDNA)

- I. Lung cancer focused panel tests via [circulating tumor DNA \(ctDNA\)](#) are considered **medically necessary** when:
 - A. The member has a new diagnosis or progression of any of the following:
 1. [Advanced](#) or metastatic lung adenocarcinoma, **OR**
 2. [Advanced](#) or metastatic large cell lung carcinoma, **OR**
 3. [Advanced](#) or metastatic squamous cell lung carcinoma, **OR**
 4. [Advanced](#) or metastatic non-small cell lung cancer (NSCLC) not otherwise specified (NOS).
- II. Lung cancer focused panel tests via [circulating tumor DNA \(ctDNA\)](#) are considered **investigational** for all other indications.

RATIONALE AND REFERENCES

Lung Cancer Focused Panel Tests via Circulating Tumor DNA (ctDNA)

National Comprehensive Cancer Network (NCCN): Non-Small Cell Lung Cancer (7.2025)

This guideline recommends biomarker testing be performed pre-treatment for patients with clinically confirmed advanced or metastatic disease of the following lung cancer pathologies: adenocarcinoma, large cell, squamous cell carcinoma, and non-small cell lung cancer not otherwise specified (p. NSCL-14, NSCL-15, NSCL-19, NSCL-H 2-7 of 8). Broad NGS panel-based testing is recommended over other modalities and smaller tests where feasible (NSCL-H, 2 of 8). Tissue-based testing and ctDNA both have high specificity and false negative rates and therefore can be used together to reduce turnaround time and increase the likelihood of finding actionable targets, however ctDNA should not be used outside of advanced or metastatic disease (NSCL-H 8 of 8). In patients who have progressed following targeted therapy, NCCN recommends

consideration of biomarker analysis to evaluate possible mechanisms of resistance (p. NSCL-H, 7 of 8).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Non-Small Cell Lung Cancer 7.2025 https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf

DEFINITIONS

1. **Advanced** cancer (advanced stages or advanced tumor or advanced/metastatic): Cancer that is unlikely to be cured or controlled with treatment. The cancer may have spread from where it first started to nearby tissue, lymph nodes, or distant parts of the body. Treatment may be given to help shrink the tumor, slow the growth of cancer cells, or relieve symptoms.
2. **Circulating tumor DNA (ctDNA)** is fragmented, tumor-derived DNA circulating in the bloodstream that is not being carried in a cell. ctDNA derives either directly from the tumor or from circulating tumor cells.
3. **Circulating Tumor Cells (CTCs)** are intact cells that have shed into the bloodstream or lymphatic system from a primary tumor or a metastasis site, and are carried around the body by blood circulation.
4. **Tumor mutational burden:** A measurement of mutations carried by tumor cells and is a predictive biomarker that is being studied to evaluate its association with response to immunotherapy.
5. **Widely metastatic:** A cancer for which local control cannot be delivered to all areas of disease (per NCCN guidelines).