

CYFRA 21-1 (Cytokeratin 19 Fragment) in Lung Cancer

Last Literature Review: November 2019 Last Update: August 2023

CYFRA 21-1 (cytokeratin 19 fragment) has been demonstrated as clinically useful in the prognostication and monitoring of non-small cell lung cancer (NSCLC). Elevated pretreatment levels may be associated with unfavorable prognosis, and decreasing levels during therapy predict an objective response to treatment. However, the level of CYFRA 21-1 cannot be used as absolute evidence for the presence or absence of disease, and results must be viewed in context of other clinical evidence.

Disease Overview

Prevalence

Lung cancer is the second most common cancer in the U.S. and the most common cause of cancer-related deaths in both men and women.

Physiology

- Cytokeratins are intermediate filament structural proteins found in the cytoskeleton of epithelial tissue.
- The two types of cytokeratins are:
 - Acidic type I
 - Basic or neutral type II
- Release of cytokeratins into the circulation occurs by numerous mechanisms, such as:
 - Cellular apoptosis
 - Abnormal mitosis
 - Spillover from proliferating cells
- Cytokeratins are detected as partially degraded, single-protein fragments or complexes, but no intact molecules.
- Elevations of cytokeratins are observed in all histologic types of NSCLC.

Prognosis/Monitoring Issues

- CYFRA 21-1 has been demonstrated as clinically useful in prognostication and monitoring.
- Elevated pretreatment CYFRA 21-1 in NSCLC is reported to be associated with unfavorable prognosis.^{1,2,3}
- Decreasing concentrations of CYFRA 21-1 in NSCLC predict objective response to treatment in advanced disease.^{4,5}

Test Interpretation

Sensitivity

Clinical sensitivity: varies by disease stage⁶

Analytic sensitivity: limit of detection is 0.5 ng/mL

Results

Possible results include:

- Elevated
- Normal (does not rule out NSCLC)

Featured ARUP Testing

[CYFRA 21-1 \(Cytokeratin 19 Fragment\), Serum 0081344](#)

Method: Quantitative Enzyme-Linked Immunosorbent Assay

- Prognostication in NSCLC
- Monitoring treatment in NSCLC

Limitations

- Test is not suitable for lung cancer screening
- Results obtained with different tests or kits cannot be used interchangeably.
- Test interference may occur with:
 - Hemolyzed specimens
 - Icteric specimens
 - Lipemic specimens
 - Interfering antibodies in specimen (human antimouse or heterophile antibodies)
- CYFRA 21-1 may also be elevated in:
 - Benign respiratory disease
 - Other cancers:
 - Urologic
 - Gastrointestinal
 - Gynecologic

References

1. Hanagiri T, Sugaya M, Takenaka M, et al. [Preoperative CYFRA 21-1 and CEA as prognostic factors in patients with stage I non-small cell lung cancer.](#) *Lung Cancer*. 2011;74(1):112-117.
2. Ono A, Takahashi T, Mori K, et al. [Prognostic impact of serum CYFRA 21-1 in patients with advanced lung adenocarcinoma: a retrospective study.](#) *BMC Cancer*. 2013;13:354.
3. Park SY, Lee JG, et al. [Preoperative serum CYFRA 21-1 level as a prognostic factor in surgically treated adenocarcinoma of lung.](#) *Lung Cancer*. 2013;79(2):156-160.
4. Ardizzoni A, Cafferata MA, Tiseo M, et al. [Decline in serum carcinoembryonic antigen and cytokeratin 19 fragment during chemotherapy predicts objective response and survival in patients with advanced nonsmall cell lung cancer.](#) *Cancer*. 2006;107(12):2842-2849.
5. Yoshimura A, Uchino J, Hasegawa K, et al. [Carcinoembryonic antigen and CYFRA 21-1 responses as prognostic factors in advanced non-small cell lung cancer.](#) *Transl Lung Cancer Res*. 2019;8(3):227-234.
6. Patel JL, Erickson A, Roberts WL, et al. [Performance characteristics of an automated assay for the quantitation of CYFRA 21-1 in human serum.](#) *Clin Biochem*. 2010;43(18):1449-1452.

Related Information

[Non-Small Cell Lung Cancer Molecular Markers](#)

ARUP Laboratories is a nonprofit enterprise of the University of Utah and its Department of Pathology. 500 Chipeta Way, Salt Lake City, UT 84108
(800) 522-2787 | (801) 583-2787 | aruplab.com | arupconsult.com