

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

Indications for Ordering

- Prognostication in non-small cell lung cancer (NSCLC)
- Monitoring treatment in NSCLC

Test Description

Quantitative enzyme-linked immunosorbent assay

Tests to Consider

Primary test

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

Related tests

Prognostication and monitoring in lung cancer

- [Carcinoembryonic Antigen 0080080](#)
- [Neuron Specific Enolase 0098198](#)
- [Squamous Cell Carcinoma Antigen, Serum 0081054](#)

Disease Overview

Prevalence

- Lung cancer is the second most common cancer in U.S.
 - 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
- Two types of cytokeratins
 - Acidic type I
 - Basic or neutral type II
- Release of cytokeratins into the circulation occurs by numerous mechanisms
 - 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 lung cancer of 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 reported to be associated with unfavorable prognosis (Hanagiri, 2011; Ono, 2013; Park, 2013)
- Decreasing concentrations of CYFRA 21-1 in NSCLC predict objective response to treatment in advanced disease (Ardizzoni, 2006)

Test Interpretation

Sensitivity

- Clinical sensitivity – varies by disease stage (Patel, 2010)
- Analytical sensitivity – limit of detection is 0.5 ng/mL

Results

- Elevated
- Normal
 - Does not rule out NSCLC

Limitations

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

References

- Ardizzoni A, Cafferata MA, 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
- Hanagiri T, Sugaya 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

- Ono A, Takahashi T, et al. Prognostic impact of serum CYFRA 21-1 in patients with advanced lung adenocarcinoma: a retrospective study. *BMC Cancer*. 2013;13(354)
- 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
- Patel JL, Erickson JA, 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