

Cytokeratin 19 Fragment (CYFRA 21-1), Serum

FOR PROGNOSIS AND TREATMENT MONITORING OF PATIENTS WITH NON-SMALL CELL LUNG CANCER

Test Highlights

- CYFRA 21-1 is the most sensitive serum tumor marker for non-small cell lung cancer.
- Serum concentrations of CYFRA 21-1 correlate with tumor burden.
- CYFRA 21-1 is an independent prognostic factor for non-small cell lung cancer.
- Decreasing concentrations of CYFRA 21-1 after chemotherapy appear to be a reliable marker of treatment efficacy.

Disease Overview

- Lung cancer is the most frequently occurring cancer worldwide and is responsible for 1.2 million deaths each year. The greatest risk factor for the development of lung cancer is cigarette smoking, which is estimated to be responsible for ~87 percent of lung cancer cases.
- The prognosis for patients with lung cancer is poor. While the five-year survival rate is ~70 percent in those diagnosed early (stage I), it becomes progressively worse with advancing stages (2 percent in stage IV). Unfortunately, the majority of patients with lung cancer have advanced disease at diagnosis.
- Lung cancers are classified histologically as small-cell or non-small cell lung cancer. Non-small cell lung cancer accounts for 75–85 percent of lung cancer cases and consists of several subtypes including squamous cell carcinomas, adenocarcinomas, and large-cell carcinomas.

Epidemiology

- 213,000 new cases of lung cancer and 160,000 deaths from lung cancer occur in the United States each year.
- Although lung cancer deaths have begun to decrease among men, the number of lung cancer deaths in women continues to increase.

Pathophysiology

- Cytokeratins are intermediate filament structural proteins found in the cytoskeleton of epithelial tissue. They are divided into two types based on sequence homology: acidic type I cytokeratins and basic or neutral type II cytokeratins. Cytokeratins are usually found as dimers composed of a type I and a type II cytokeratin, which are further organized into filamentous structures by forming tetramers. The release of cytokeratins into circulation likely occurs by numerous mechanisms such as cellular apoptosis, abnormal mitosis, or spill-over from proliferating cells. When present, cytokeratins are detected as partially degraded, single-protein fragments or complexes and not as intact molecules.
- Elevated serum concentrations of specific cytokeratins are observed in patients with lung cancer of all histologic types. A fragment of cytokeratin 19, cytokeratin fragment 21-1 (CYFRA 21-1), has been extensively studied in patients with non-small cell lung cancer and has been demonstrated to be clinically useful.

Indications for Ordering

- Determining prognosis in patients with non-small cell lung cancer.
- Monitoring treatment of non-small cell lung cancer.

Clinical Utility

- Among tumor marker tests for non-small cell lung cancer, CYFRA 21-1 has consistently been shown to have the highest diagnostic sensitivity (~70 percent). In a prospective study of 211 patients with newly diagnosed, non-small cell lung cancer (stages I-IV), the sensitivity of CYFRA 21-1 determined after diagnosis but before treatment was 76 percent.¹ In another study of 180 patients suspected of having lung cancer, CYFRA 21-1 detected 65 percent of the cancers that were not detected by bronchoscopy and increased the negative predictive value for malignancy to 88 percent compared to 72 percent with bronchoscopy alone.²
- CYFRA 21-1 is a prognostic marker in patients with non-small cell lung cancer. A meta-analysis of 2,063 patients (85 percent ≥stage IIIa) concluded that an elevated pre-treatment CYFRA 21-1 concentration was an independent and unfavorable prognostic determinant at 12 and 18 months in all patients studied.³ The same was true at one and two years for patients who did not have surgical treatment and for those who did, respectively.
- A study of 341 pre-operative stage I non-small cell lung cancer patients reported a significant increase in 5-year survival in those with normal pre-operative CYFRA 21-1 concentrations (92.8 percent) versus those with elevated values (75.4 percent).⁵
- Decreasing concentrations of CYFRA 21-1 have been shown to predict objective response and survival in patients with advanced non-small cell lung cancer. A prospective study of 117 patients with advanced (stage III–IV) nonresectable disease reported that a ≥20 percent reduction in CYFRA 21-1 from baseline values after two cycles of chemotherapy was achieved in 81 percent of patients with an objective response compared to 45 percent of non-responders.⁴ The responders also had a significantly longer median survival time (11 months) when compared to non-responders (six months).

Limitations

- This test is not suitable for lung cancer screening in either asymptomatic or high-risk individuals (e.g., smokers).
- CYFRA 21-1 may also be elevated in benign respiratory disease, as well as in urological, gastrointestinal, and gynecological cancers.

Methodology

- CYFRA 21-1 is measured using a commercially available enzyme-linked immunosorbent assay (Fujirebio Diagnostics AB, Gothenburg, Sweden). Fujirebio Diagnostics, Inc. received FDA 510 (k) clearance for this assay in May 2011.
- A reference interval study conducted by ARUP Laboratories using serum samples collected from 150 healthy volunteers (75 males, 75 females) aged 19–60 years identified a CYFRA 21-1 concentration of 2.3 ng/mL as the upper 97.5th percentile.

References

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Test Information

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For specific collection, transport, and testing information, refer to the ARUP website at www.aruplab.com.

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at www.arupconsult.com.

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