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.
  o 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
  o Acidic type I
  o Basic or neutral type II
• Release of cytokeratins into the circulation occurs by numerous mechanisms
  o Cellular apoptosis
  o Abnormal mitosis
  o 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
  o 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
  o Hemolyzed specimens
  o Icteric specimens
  o Lipemic specimens
  o Interfering antibodies in specimen (human anti-mouse or heterophile antibodies)
• CYFRA 21-1 may be elevated in
  o Benign respiratory disease
  o Other cancers
    ▪ Urologic
    ▪ Gastrointestinal
    ▪ Gynecological

References