

Hepatocellular Carcinoma Serum Markers

Indications for Ordering

- Alpha fetoprotein (AFP), total and L3 percent
 - Surveillance in conjunction with abdominal ultrasound for early detection of hepatocellular carcinoma (HCC) in high-risk groups
 - Posttreatment monitoring when pretreatment concentration was elevated
- Des-gamma-carboxy prothrombin (DCP)
 - Surveillance in conjunction with abdominal ultrasound for early detection of HCC in high-risk groups
 - May be used in monitoring if pretreatment levels were elevated

Test Description

- Alpha Fetoprotein, Total and L3 Percent
 - Quantitative liquid chromatography/immunoassay
 - Alpha fetoprotein L3 isoform (AFP-L3%) is calculated as a percentage of AFP-L3 in the total AFP concentration
- Des-gamma-carboxy Prothrombin
 - Quantitative liquid chromatography/immunoassay

Tests to Consider

Primary tests

[Alpha Fetoprotein, Total and L3 Percent 0081208](#)

- Surveillance and monitoring of HCC

[Des-gamma-carboxy Prothrombin 0081312](#)

- Surveillance and monitoring of HCC

Related tests

[Alpha Fetoprotein, Serum \(Tumor Marker\) 0080428](#)

- Surveillance and monitoring of HCC
- Less specific than test that includes AFP-L3 isoform

[Hepatocellular Carcinoma Tumor Marker Panel 0081326](#)

- Acceptable panel for surveillance and monitoring of HCC
 - Includes AFP total, AFP-L3%, and DCP

Disease Overview

Prevalence and/or incidence

- 4-11/100,000 (U.S. and Europe)
- >26,000 new cases per year (NCCN 2011)

Screening/detection

- Disease is often discovered at late stage due to nonspecific symptoms
 - Poor prognosis at this point
- Possible role for surveillance of high-risk individuals using combined serum marker testing and abdominal ultrasound to detect earlier disease

Biology

- AFP-L3
 - AFP has 3 isoforms – L1, L2, L3
 - L3 isoform is expressed by malignant hepatocytes
 - L3 isoform has highest affinity for lectin from *Lens culinaris*, which makes it possible to differentiate L3 from other isoforms
- DCP
 - Also referred to as PIVKA-II (protein induced by vitamin K absence or antagonist II)
 - Nonfunctional prothrombin
 - Results from lack of carboxylation of 10 glutamic acid residues
 - Vitamin K dependent carboxylase, which catalyzes this reaction in many HCCs, is absent

Test Interpretation

Sensitivity/specificity

- Clinical sensitivity/specificity
 - AFP-L3%
 - L3% $\geq 10\%$
 - Relative risk (RR) – 43.3% (95% CI: 31.4-55.4%)
 - L3% $< 10\%$
 - RR – 4.1% (95% CI: 1.6-6.6%)
 - DCP
 - DCP ≥ 7.5
 - RR – 36.5% (95% CI: 23.5-49.6%)
 - DCP < 7.5
 - RR – 7.6% (95% CI: 4.4-10.8%)
- Analytical sensitivity
 - AFP and DCP – 0.1 ng/mL
- Analytical specificity – none known

Results

- Normal cutoffs
 - AFP – 0-15 ng/mL
 - AFP-L3% – 0-9.9%
 - DCP – 0-7.4 ng/mL

Limitations

- Not all HCCs secrete AFP and/or DCP
 - Test is not useful for monitoring if pretreatment levels were not elevated
- False-positive result may occur in the following clinical contexts
 - AFP-L3%
 - Pregnancy
 - Age <1 year
 - Acute fulminant hepatitis
 - Cirrhosis
 - DCP
 - Obstructive jaundice
 - Intrahepatic cholestasis
 - Drugs (eg, warfarin)