

# 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  $\geq 7.5$ 
      - 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)