Overview

Useful For
Risk assessment of patients with chronic liver disease for development of hepatocellular carcinoma

Profile Information

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Reporting Name</th>
<th>Available Separately</th>
<th>Always Performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>L3AFP</td>
<td>AFP-L3% and Total AFP, S</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>DCP</td>
<td>Des-Gamma-Carboxy Prothrombin, S</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Method Name
Isotachophoresis with Laser-Induced Fluorescence

NY State Available
Yes

Specimen

Specimen Type
Serum

Specimen Required
Container/Tube:

Preferred: Red top

Acceptable: Serum gel

Specimen Volume: 0.5 mL

Forms
If not ordering electronically, complete, print, and send a Gastroenterology and Hepatology Client Test Request (T728) with the specimen.

Specimen Minimum Volume
0.25 mL

Reject Due To

<table>
<thead>
<tr>
<th>Condition</th>
<th>Acceptance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemolysis</td>
<td>Mild OK; Gross reject</td>
</tr>
<tr>
<td>Lipemia</td>
<td>Mild OK; Gross OK</td>
</tr>
<tr>
<td>Icterus</td>
<td>NA</td>
</tr>
<tr>
<td>Other</td>
<td>NA</td>
</tr>
</tbody>
</table>
Specimen Stability Information

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum</td>
<td>Frozen (preferred)</td>
<td>90 days</td>
</tr>
<tr>
<td></td>
<td>Refrigerated</td>
<td>5 days</td>
</tr>
</tbody>
</table>

Clinical and Interpretive

Clinical Information

Worldwide, hepatocellular carcinoma is the third leading cause of death from cancer. While hepatocellular carcinoma can be treated effectively in its early stages, most patients are not diagnosed until they are symptomatic and at higher grades and stages, which are less responsive to therapies. Alpha-fetoprotein (AFP) is the standard serum tumor marker utilized in the evaluation of suspected hepatocellular carcinoma. However, increased serum concentrations of AFP might be found in chronic hepatitis and liver cirrhosis, as well as in other tumor types (e.g., germ cell tumors), decreasing the specificity of AFP testing for hepatocellular carcinoma. Furthermore, AFP is not expressed at high levels in all hepatocellular carcinoma patients, resulting in decreased sensitivity, especially in potentially curable small tumors.

L3AFP:

AFP is differentially glycosylated in several hepatic diseases. For example, UDP-alpha-1→6-fucosyltransferase is differentially expressed in hepatocytes following malignant transformation. This enzyme incorporates fucose residues on the carbohydrate chains of AFP. Different glycosylated forms of AFP can be recognized following electrophoresis by reaction with different carbohydrate-binding plant lectins. The fucosylated form of serum AFP that is most closely associated with hepatocellular carcinoma is recognized by a lectin from the common lentil. This is designated as AFP-L3 (third electrophoretic form of lectin-reactive AFP). AFP-L3 is most useful in the differential diagnosis of individuals with total serum AFP < or =200 ng/mL, which may result from a variety of benign pathologies, such as chronic liver diseases.

DCP:

Des-gamma-carboxy prothrombin (DCP), also known as the protein induced by vitamin K absence or antagonist II (PIVKA-II), is an abnormal form of the coagulation protein, prothrombin. DCP is a nonfunctional prothrombin resulting from a lack of carboxylation of 10 glutamic acid residues in the N-terminal portion of the molecule. In normal liver, prothrombin undergoes post-translational carboxylation before release into the peripheral blood. The carboxylation converts specific amino-terminal glutamic acid residues to gamma-carboxyglutamic acid. The vitamin K dependent carboxylase responsible for the carboxylation is absent in many hepatocellular carcinoma (HCC) cells, and an abnormal prothrombin with all or some of unconverted glutamic acid is secreted. Therefore, this noncarboxylated form (DCP) has been used as an HCC biomarker.

DCP is considered a complementary biomarker to alpha fetoprotein AFP and AFP-L3% for assessing the risk of developing HCC. The elevation of both AFP-L3% and DCP indicate progression of HCC, albeit they reflect different features of the progression. In a prospective study of patients in the United States with an established diagnosis of HCC, the sensitivities for AFP, AFP-L3%, and DCP were 68%, 62%, and 73%, respectively. When the 3 markers were combined, the sensitivity was 86%. In another study, DCP levels were shown to correlate with tumor size and metastatic HCC. In this study, compared to AFP and AFP-L3%, DCP had the highest sensitivity (87%) and the...
highest positive predictive value (87%) in patients with HCC due to chronic hepatitis B and C infections. A number of studies have shown that elevated serum DCP is significantly related to portal vein invasion and/or intrahepatic metastasis, which significantly affect prognosis for patients with HCC.

DCP can be elevated in other conditions besides HCC. Conditions such as obstructive jaundice, intrahepatic cholestasis causing chronic decrease in vitamin K, and ingestion of drugs such as warfarin or wide-spectrum antibiotics can result in high concentrations of DCP. In addition, 25% to 50% of patients with HCC will have a DCP value within the reference range. Because of this, a normal DCP value does not rule out HCC.

**Reference Values**

- **TOTAL AFP:** <4.7 ng/mL
- **L3AFP:** <10%
- **DCP:** <7.5 ng/mL

**Interpretation**

**L3AFP:**

Alpha-fetoprotein (AFP)-L3 \(\geq 10\%\) is associated with a 7-fold increased risk of developing hepatocellular carcinoma. Patients with AFP-L3 \(\geq 10\%\) should be monitored more intensely for evidence of hepatocellular carcinoma according to current practice guidelines.

Total serum AFP \(>200\) ng/mL is highly suggestive of a diagnosis of hepatocellular carcinoma. In patients with liver disease, a total serum AFP of \(>200\) ng/mL is near 100% predictive of hepatocellular carcinoma. With decreasing total AFP levels, there is an increased likelihood that chronic liver disease, rather than hepatocellular carcinoma, is responsible for the AFP elevation.

Based on a retrospective study at Mayo Clinic, for patients with total AFP levels \(<\leq 200\) ng/mL, AFP-L3 specificity approaches 100% for hepatocellular carcinoma when its percentage exceeds 35% of the total AFP.\(^{(4)}\)

AFP concentrations over 100,000 ng/mL have been reported in normal newborns, and the values rapidly decline in the first 6 years of life.

**DCP:**

In patients with an elevated des-gamma-carboxy prothrombin (DCP) result \(\geq 7.5\) ng/mL, the risk of developing hepatocellular carcinoma (HCC) is 36.5% (95% CI 23.5%-49.6%). The risk of developing HCC with a negative DCP result \(<7.5\) ng/mL) is 7.6% (95% CI 4.4%-10.8%).

**Cautions**

Serum markers are not specific for malignancy, and values may vary by method. Do not interpret alpha-fetoprotein (AFP), AFP-L3, and des-gamma-carboxy prothrombin (DCP) levels as absolute evidence of the presence or absence of malignant disease. Results should be used in conjunction with information from the clinical evaluation of the patient, cytology, and imaging procedures.

Values obtained with different assay methods or kits cannot be used interchangeably.

Some patients who have been exposed to animal antigens, either in the environment or as part of treatment or imaging procedures, may have circulating anti-animal antibodies present. These antibodies may interfere with the assay reagents to produce unreliable results in the AFP-L3 and DCP assays.
Test results for AFP are not interpretable if the patient is pregnant.

DCP-producing tumors other than hepatocellular carcinoma can show elevated DCP values. Liver disease caused by other etiologies such as alcohol-induced liver disease, hemochromatosis, Wilson disease, autoimmune hepatitis, and steatohepatitis have not been studied with the DCP assay.

Medications containing vitamin K preparations may cause a negative bias with DCP values. Medications containing vitamin K antagonist or antibiotic may cause a positive bias with DCP values.

Clinical Reference
5. Package insert: LBA AFP-L3, Wako Diagnostics, Richmond, VA. 06.1.24K02

Performance

Method Description
Testing is performed using the uTASWako i30 instrument and the test system reagents.

L3AFP:

Total alpha-fetoprotein (AFP) is measured by laser-induced fluorescence, with separation of the lentil lectin-reactive AFP-L3 and lectin nonreactive forms of AFP by isotachophoresis of their immune-complexes. Results are expressed as the percent ratio of AFP-L3 to total AFP. (Package insert: uTASWako i30 AFP-L3, Wako Diagnostics, Richmond, VA)
DCP:

Sample is added to the reagent well with the fluorescent dye labeled anti-human prothrombin antibody (mouse monoclonal) to form the primary immunocomplex. The second labeled antibody solution, anion-conjugated anti-human des-gamma-carboxy prothrombin (DCP) antibody (mouse monoclonal), is concentrated by isotachophoresis when voltage is applied. The concentrated anion-conjugated antibody then reacts with the primary immunocomplex to form the secondary immunocomplex. This secondary complex is further concentrated during isotachophoresis and is separated from unbound fluorescent dye-labeled antibody by capillary gel electrophoresis. The remaining dye labeled DCP is measured by laser-induced fluorescence. The concentration of DCP in the specimen is directly proportional to the amount of fluorescence. (Package insert: uTAS Wako i30 DCP, version 11.03.08K02. Wako Diagnostics, Richmond, VA)

PDF Report
No

Day(s) and Time(s) Test Performed
Monday, Wednesday, Friday; 10 a.m.

Analytic Time
Same day/1 day

Maximum Laboratory Time
3 days

Specimen Retention Time
14 months

Performing Laboratory Location
Rochester

Fees and Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

CPT Code Information
82107
83951

LOINC® Information

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Test Order Name</th>
<th>Order LOINC Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCCPR</td>
<td>Hepatocellular Carcinoma Risk Panel</td>
<td>In Process</td>
</tr>
</tbody>
</table>

Document generated August 31, 2019 at 2:21pm CDT
### Test Definition: HCCPR

**Hepatocellular Carcinoma Risk Panel**

<table>
<thead>
<tr>
<th>Result ID</th>
<th>Test Result Name</th>
<th>Result LOINC Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAFP</td>
<td>Total AFP, S</td>
<td>1834-1</td>
</tr>
<tr>
<td>DCP</td>
<td>Des-Gamma-Carboxy Prothrombin, S</td>
<td>34444-0</td>
</tr>
<tr>
<td>L3</td>
<td>%L3</td>
<td>42332-7</td>
</tr>
<tr>
<td>INT67</td>
<td>Interpretation</td>
<td>59462-2</td>
</tr>
</tbody>
</table>