

# AFP-L3 Percent in Serum (Includes Total Alpha-Fetoprotein)

## *FOR RISK ASSESSMENT OF HEPATOCELLULAR CARCINOMA IN PATIENTS WITH CHRONIC LIVER DISEASE*

### Test Highlights

- Concentrations of both total alpha-fetoprotein (AFP) and AFP-L3% are quantified in a single serum sample. The concentration of AFP-L3% is considered elevated (positive) if it is greater than 10% of the total AFP.
- Elevated AFP-L3% values are associated with a seven-fold increase in the risk of developing hepatocellular carcinoma (HCC) within the next 21 months.
- AFP-L3% becomes elevated three to 21 months before HCC can be detected by standard imaging techniques.
- While total AFP may be related to clinical stage, the AFP-L3% is an indicator of biological behavior (aggressiveness) of HCC. AFP-L3%-positive HCC has the potential for rapid growth and early distant metastasis.
- The high specificity of AFP-L3% makes it a desirable marker for monitoring patients after completion of therapy. A positive result that subsequently turns negative for AFP-L3% is usually indicative of successful treatment of HCC.

### Clinical Background

- HCC incidence in the United States has increased substantially over the last few decades; approximately 24,000 new cases occur every year. This highlights an increasing need for specific biomarkers to assist in risk assessment, surveillance, and early detection of HCC.
- The National Cancer Institute projects 3% to 5% annual increases in the prevalence of HCC.
- Patients with chronic hepatitis B or C, hemochromatosis, or cirrhosis are at highest risk of developing HCC.
- A 2010 CDC report found a total of 48,596 new cases of HCC during 2001–2006 and an average annual incidence rate of 3/100,000 persons.
- This FDA-cleared test measures both total AFP and the percentage of the L3 isoform. There are three isoforms of AFP, each with varying affinity for the lectin from *Lens culinaris*. The high affinity of the L3 isoform, which is expressed by malignant hepatocytes, for this lectin is exploited to differentiate it from L1 and L2 isoforms.
- The cutoff point for “abnormal” changes the sensitivity and the specificity. Using a 10 ng/mL cutoff point for total AFP gives a sensitivity of 79%, but a specificity of only 62%. Using a 10% AFP-L3% cutoff, the sensitivity is 51%, but the specificity is 92%. While many conditions may elevate the total concentration of AFP, clinical data shows that increased L3% was 92% specific for those patients with AFP-secreting HCC. Nonmalignant liver disease does not appear to increase AFP-L3% over the 10%-positive cutoff point. Elevations of AFP-L3% can be used as a risk marker for HCC and indicate the need for a more careful evaluation for evidence of HCC according to the existing HCC practice guidelines.
- A 2008 study reported that AFP-L3 demonstrated 90% specificity at 56% sensitivity (56% positive predictive value) for HCC in patients with chronic hepatitis or cirrhosis.

### Limitations

- Not all liver cancers are AFP-secreting, and AFP may be elevated due to germ-cell tumors and other carcinomas.
- Viral infections, cirrhosis, and other liver diseases may elevate AFP.
- Samples from patients who are pregnant, less than one year of age, or who have acute or fulminate hepatitis can show elevated values of AFP-L3% and total AFP.

### Methodology

- AFP-L3 isoform is produced in HCC cells by attachment of an  $\alpha$ 1,6 fucose residue on N-acetylglucosamine of the carbohydrate chain on AFP. This carbohydrate complex reacts with *Lens culinaris* agglutinin (LCA). The AFP-L3% is a ratio of the LCA-reactive AFP to the total AFP.
- The  $\mu$ TASWako<sup>®</sup> AFP-L3 assay uses a microfluidic electrophoretic separation process on a chip. The sample and antibody reagents are dispensed into the chip and form the primary immunocomplex. Voltage is applied to the chip, and a DNA-labeled secondary antibody moves to the anode and is concentrated by isotachopheresis. This concentrated secondary antibody reacts with the primary immunocomplex and forms the secondary immunocomplex. This secondary immunocomplex is further concentrated during isotachopheresis to the anode and is separated from unbound reagent by capillary gel electrophoresis. Affinity for LCA within the gel retards the migration of AFP-L3 complexes relative to AFP-L1, causing two distinct signal peaks that are detected by laser-induced fluorescence to quantify the concentration of AFP in the sample. AFP-L3% is calculated as a percentage of AFP-L3 in the total AFP concentration.

### Related Tests

- Alpha Fetoprotein, Serum (Tumor Marker) (0080428) may be ordered if only the total AFP without the AFP-L3% is desired.
- Des-gamma-carboxy Prothrombin (0081312)
- Hepatocellular Carcinoma Tumor Marker Panel (0081326)

### References

1. Debruyne EN, Delanghe JR. Diagnosing and monitoring hepatocellular carcinoma with alpha-fetoprotein: new aspects and applications. *Clin Chim Acta*. 2008;395(1-2):19-26.
2. Toyoda H, et al. Prognostic significance of simultaneous measurement of three tumor markers in patients with hepatocellular carcinoma. *Clin Gastroenterol Hepatol*. 2006;4:111-117.

3. Carr B, et al. Clinical evaluation of Lens culinaris agglutinin-reactive alpha-fetoprotein and des-gamma-carboxy prothrombin in histologically proven hepatocellular carcinoma in the United States. *Dig Dis Sci*. 2007;52:776-782.
4. Durazo F, et al. Des-gamma-carboxyprothrombin, alpha-fetoprotein, and AFP-L3 in patients with chronic hepatitis, cirrhosis, and hepatocellular carcinoma. *J Gastroenterol Hepatol*. 2008;23(10):1541-1548.
5. AFP-L3% [package insert]. Richmond, VA: Wako Diagnostics; 2006.

## Test Information

### 0081208 Alpha Fetoprotein, Total and L3 Percent

For specific collection, transport, and testing information, refer to the ARUP website at [www.aruplab.com](http://www.aruplab.com).

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at [www.arupconsult.com](http://www.arupconsult.com).

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