

# Diagnosis and Management of Hepatocellular Carcinoma: 2009 Update

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## Abstract

Hepatocellular carcinoma (HCC) is the fifth commonest cancer in the world and represents a rapidly growing source of liver-associated morbidity and mortality in the United States. Improvements in surveillance strategies and diagnostic imaging techniques have led to an increasing capacity to establish a diagnosis of HCC without tissue confirmation. Liver transplantation remains the treatment of choice for patients with decompensated liver disease and tumors within Milan criteria. Sorafenib and other new molecular targeted therapies provide new hope for patients with advanced, unresectable HCC. This review summarizes recent evidence addressing screening, diagnosis, and management of HCC.

## Target Audience

This activity has been designed to meet the educational needs of hepatologists, gastroenterologists, physician assistants, and nurse practitioners involved in the management of chronic liver disease.

## Goal Statement

To provide important clinical data on the management of hepatocellular carcinoma (HCC)

## Educational Objectives

Upon completion of this activity, participants should be better able to:

- Review the epidemiology and etiology of HCC
- Describe the latest treatment advances
- Discuss the latest treatment algorithms for the management of HCC

## Accreditation Statement

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Education (ACCME) through the joint sponsorship of Purdue University School of Pharmacy and Chronic Liver Disease Communications. Purdue University School of Pharmacy, an equal access/equal opportunity institution, is accredited by the ACCME to provide continuing medical education for physicians.

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## Diagnosis and Management of Hepatocellular Carcinoma: 2009 Update

### Introduction

Hepatocellular carcinoma (HCC) is the fifth most common cancer in the world and is an increasingly common complication of chronic liver disease in the United States. Population studies suggest a rising incidence of HCC from 1.4 per 100,000 between 1975 and 1977 to 3.0 per 100,000 between 1996 and 1998 to 6.4 between 2001 and 2005, which is now associated with the fastest growing death rate among cancers in the United States.<sup>1-3</sup> The leading risk factors for HCC vary by geography but in the United States are associated with cirrhosis in 50%–80% of patients, predominantly from chronic hepatitis C infection and alcoholic liver disease, and also chronic hepatitis B infection, which represents a risk factor for HCC development independent of cirrhosis.<sup>4</sup> The natural history of HCC is frequently indolent in its early phases, particularly if it is identified as a single nodule during surveillance testing, although it may be determined by such factors as tumor size, number of tumor nodules, vascular invasion, and liver synthetic function.

### Surveillance

While screening represents the use of diagnostic tests to detect unsuspected disease in asymptomatic individuals, surveillance is distinguished by an ongoing, systematic collection and analysis of diagnostic tests that lead to specific actions to prevent or control a disease. Recommended surveillance for HCC consists of a combination of serum alpha-fetoprotein (AFP) and abdominal ultrasound every 6–12 months.<sup>5</sup> Although 6 months is preferred due to estimated tumor doubling times (eg, 4–6 months), one-year intervals appear to be similarly effective. Due to the limitations of abdominal ultrasound related to body habitus, operator dependence, and decreased sensitivity in cirrhotic livers, contrast-enhanced computed tomography (CT) scan or magnetic resonance imaging (MRI) should be considered in individuals with a clinical suspicion for HCC, such as elevated AFP, abnormal lesion on ultrasound, or if ultrasound images are unable to exclude a hepatoma. Among high-risk individuals with cirrhosis awaiting liver transplantation, screening with dynamic triple phase helical CT may be cost effective<sup>6</sup> but should be avoided in individuals requiring long-term surveillance with consideration of cumulative radiation exposure and false-positive findings. Serum AFP has low sensitivity for detecting HCC and may be expressed in individuals

with chronic liver disease in the absence of HCC. Therefore, serum AFP should not be used alone for HCC surveillance. Only one-third of individuals with HCC have serum AFP levels exceeding 100 ng/mL.<sup>7</sup> However, significantly elevated AFP levels greater than 200 ng/mL are associated with a high positive predictive value for a diagnosis of HCC.<sup>8</sup> Other screening markers, such as glycosylated AFP (L3 fraction), alpha fucosidase, and des-gamma-carboxy prothrombin (DGCP), have been described, but inadequate data are available to recommend their use in clinical practice.

### Patients in whom HCC surveillance is recommended<sup>5</sup>

#### Hepatitis B carriers

- Asian men  $\geq$ 40 years
- Asian women  $\geq$ 50 years
- All cirrhotic hepatitis B carriers
- Family history of HCC
- Black patients over age 20
- Other non-cirrhotic hepatitis B carriers (risk of HCC varies based on severity of underlying disease, current and past inflammatory activity, and hepatitis B virus DNA levels)

#### Non-hepatitis B virus cirrhosis

- Hepatitis C
- Alcoholic cirrhosis
- Genetic hemochromatosis
- Primary biliary cirrhosis
- Other etiologies of cirrhosis (alpha-1 antitrypsin deficiency, nonalcoholic steatohepatitis, autoimmune hepatitis)\*

*\*Inadequate data on benefit of surveillance*

### Table 1

Surveillance is recommended for all high-risk individuals (Table 1) and is ideally performed in a structured process that includes predetermined pathways for recall and follow-up of abnormal findings. Identifying at-risk individuals requires an assessment of the threshold of HCC incidence at which surveillance is likely to be effective. Using cost-efficacy and decision analytic models, HCC surveillance is found to be effective when the HCC incidence exceeds 1.5% per year in cirrhotic patients or 0.2% per year in non-cirrhotic patients with chronic hepatitis B infection.<sup>5</sup> On this basis, surveillance is recommended for all

patients with a diagnosis of cirrhosis with particular attention to those with hepatitis B or C infection, alcoholic liver disease, primary biliary cirrhosis, or genetic hemochromatosis and non-cirrhotic patients with chronic hepatitis B infection, including Asian women  $\geq 50$  years, Asian men  $\geq 40$  years, black patients over age 20, and those with a family history of HCC. Although a number of observational studies have suggested an improved survival with surveillance, only one randomized, controlled trial has demonstrated survival advantage to individuals undergoing HCC surveillance with AFP plus abdominal ultrasound every 6 months. In a large Chinese study involving 18,816 patients with current or prior hepatitis B infection, despite less than 60% adherence to recommended surveillance, individuals randomized to surveillance had a 37% reduction in HCC-specific mortality.<sup>9</sup>

### Diagnosis

Hepatocellular carcinoma is frequently asymptomatic but may present with right upper quadrant pain, weight loss, and worsening liver enzymes or, less commonly, anemia, intra-abdominal hemorrhage, or complications of portal hypertension.<sup>10</sup> The diagnosis of HCC is typically established on a dynamic triple-phase contrast-enhanced CT or MRI performed in response to an abnormal screening test or heightened clinical suspicion. The presence of characteristic vascular pattern (arterial phase enhancement with portal venous washout) has favorable test characteristics including high sensitivity (90%) and specificity (95%) and should be considered diagnostic of HCC. Although more than 70% of individuals with HCC have these radiologic features, those who have an atypical vascular pattern should undergo an imaging-guided biopsy.

Suggested management of liver masses and HCC in cirrhosis

Liver mass on ultrasound in a patient with cirrhosis	Mass <1 cm	Diagnosis:	• Low likelihood of being HCC; therefore, no specific diagnostic tests		
		Follow-up	<ul style="list-style-type: none"> <li>• Repeat imaging study every 3 months</li> <li>– If no growth in 1–2 years → no HCC</li> <li>– If growth, treat as HCC</li> </ul>		
	Mass 1 cm - 2 cm	Diagnosis:	Two dynamic imaging studies (ultrasound, CAT scan, or MRI)	• Both with typical vascular pattern	• Treat as HCC
				• One typical and the other atypical	• Biopsy of mass
				• Both atypical	• Biopsy of mass
		Follow-up after biopsy	Biopsy confirms HCC	• Treat as HCC	
	Non-diagnostic		<ul style="list-style-type: none"> <li>• Repeat imaging study every 3 months</li> <li>• If no growth in 1–2 years → no HCC</li> <li>• If growth, treat as HCC</li> </ul>		
	Mass >2 cm	Diagnosis:	One dynamic imaging study (ultrasound, CAT scan, or MRI)	• Typical vascular pattern	• Treat as HCC
				• Atypical vascular pattern	• Biopsy of mass
		Follow-up after biopsy	Biopsy confirms HCC	• Treat as HCC	
Non-diagnostic			<ul style="list-style-type: none"> <li>• Repeat imaging study every 3 months</li> <li>– If no growth in 1–2 years → no HCC</li> <li>– If growth, treat as HCC</li> </ul>		

Figure 1

The approach to HCC diagnosis is largely determined by tumor size (Figure 1). For lesions greater than 2 cm in diameter in an individual with known cirrhosis or chronic hepatitis B infection, the likelihood of HCC is high, and a diagnosis can be established in the absence of a liver biopsy if serum AFP is greater than 200 ng/mL and a characteristic radiologic pattern is seen on one dynamic contrast-enhanced imaging study. If the vascular pattern is atypical or the serum AFP is less than 200 ng/mL, a biopsy should be performed. For lesions measuring 1 cm–2 cm in diameter in a patient with known cirrhosis or chronic hepatitis B, the likelihood of HCC also remains high. However, a diagnosis of HCC is established by the presence of a characteristic radiologic pattern on 2 dynamic imaging studies (CT and MRI). In the absence of typical vascular pattern on both studies, a biopsy is recommended, although the unique challenges of obtaining a diagnostic sample and differentiating between dysplasia, early or small HCC, and well-differentiated HCC highlight the need

for expert pathology review in these cases. If the biopsy is non-diagnostic, surveillance imaging every 3 months should be performed. Mass lesions measuring less than 1 cm in diameter are unlikely to represent HCC, although radiographically evident nodules in a cirrhotic patient bear malignant potential and should be monitored with dynamic contrast-enhanced imaging studies every 3 months. If stable over 2 years, a return to standard surveillance interval is appropriate. Interval growth on follow-up imaging is highly suggestive of HCC. Due to geographical and institutional differences in radiology and pathology expertise, clinicians should utilize best local practices in application of these guidelines.

### Staging

Staging for HCC may assist clinicians in assessing prognosis and determining the treatment approach (Figure 2). Recognizing the importance of such variables as performance status and liver synthetic function on prognosis, traditional

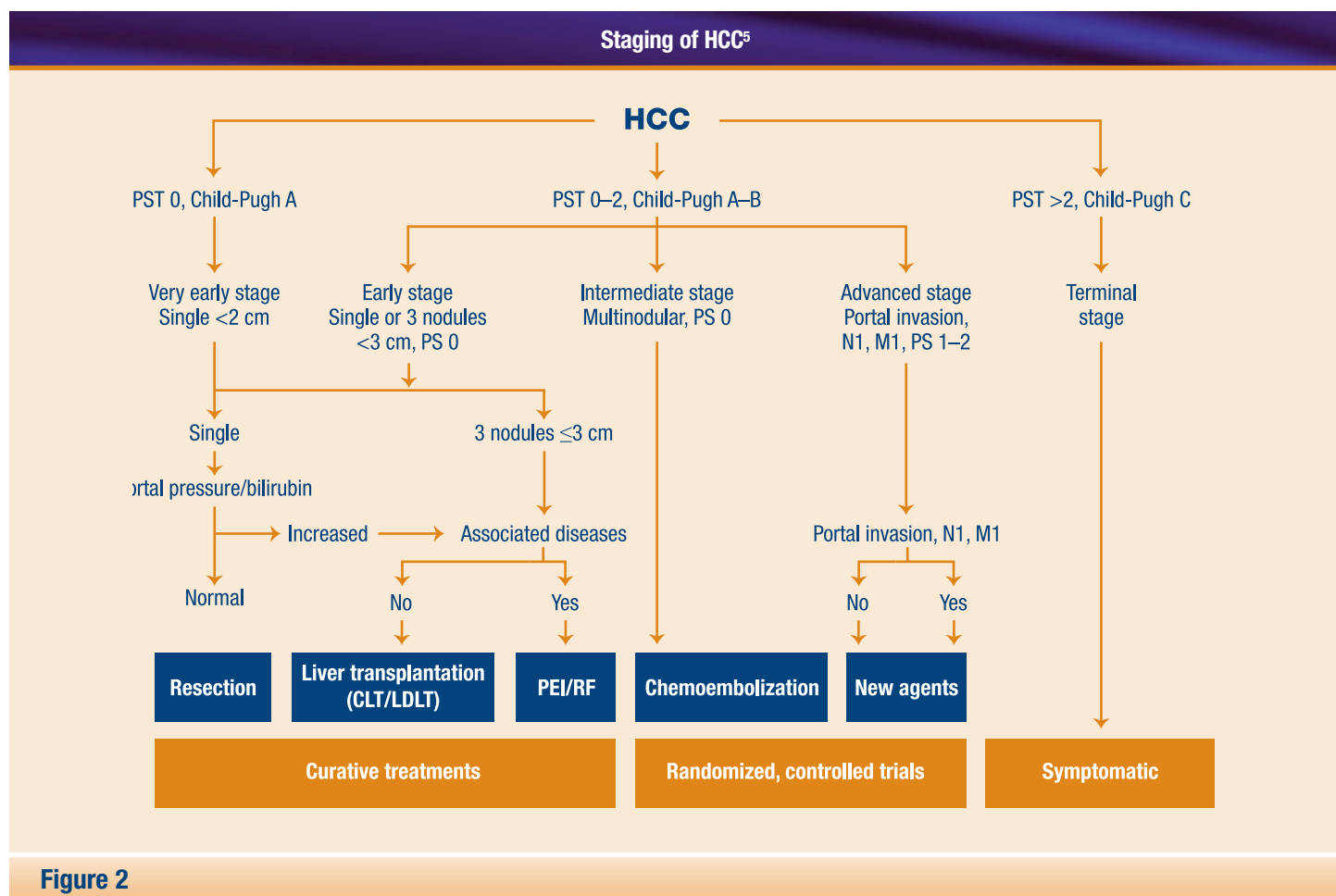


Figure 2

histopathologic scoring systems, such as the tumor-node-metastasis (TNM) system, lack adequate prognostic value for standard clinical use. As such, no single system is universally accepted for this purpose, although the 5-stage Barcelona Clinic Liver Cancer (BCLC) system is one that has been adopted by many in the United States due to its incorporation of such elements as tumor size and pathology, performance status using World Health Organization (WHO) criteria, liver synthetic function based on Child-Turcotte-Pugh (CTP) score, and portal hypertension and has the main advantage of directing clinicians to stage-specific treatment strategies.<sup>11,12</sup> “Very early stage” disease is characterized by a single lesion less than 2 cm in diameter in a healthy individual with CTP Class A disease without portal hypertension or vascular invasion and is best treated with local tumor resection, although radiofrequency ablation (RFA) may be considered depending on tumor location and local expertise. Those with “early stage” disease have CTP Class A or B disease with up to 3 tumors up to 3 cm in diameter each and may be treated with local tumor resection, liver transplantation, or ablative therapy with consideration of performance status, portal hypertension, and liver synthetic function. Patients with “intermediate stage” disease represent those patients who have compensated CTP Class A or B disease without vascular invasion or tumor-specific symptoms and have features that are beyond the definitions for “early stage” disease. Transarterial chemoembolization (TACE) is the preferred treatment of choice and may improve 2-year survival, although clinical trials may be considered for those who fail to respond to initial therapy. Individuals with “advanced stage” disease have CTP Class A or B cirrhosis but have evidence of extrahepatic spread or portal venous invasion and may have evidence of tumor-specific symptoms. Although TACE has been used in selected individuals, these patients may represent appropriate candidates for sorafenib therapy or enrollment in clinical trials. “Terminal stage” disease has a very poor prognosis with 1-year survival lower than 10%, and the treatment approach should be focused on palliation of tumor-related symptoms and complications.

## Treatment

Rapid advancement in the development of radiologic and surgical therapies over the past decade has contributed significantly to current treatment guidelines and will likely continue to evolve with the emergence of novel molecular-targeted therapies, which may transform the management of advanced unresectable HCC. The treatment of HCC requires

careful consideration of the medical status of individual patients, including an assessment of performance status, liver synthetic function, and the presence of compensated or decompensated cirrhosis. Due to significant geographical and institutional differences in expertise, patients with HCC are ideally referred to centers with multidisciplinary teams including hepatologists, interventional radiologists, transplant surgeons, oncologists, and pathologists. In general, liver transplantation remains the best treatment option for those individuals with decompensated cirrhosis and a solitary tumor less than 5 cm in diameter or up to 3 tumors each up to 3 cm in diameter. Conversely, local tumor resection represents the treatment of choice for solitary tumors in non-cirrhotic patients. Current treatment strategies include surgical resection, ablative therapies, such as radiofrequency ablation (RFA) or percutaneous ethanol injection (PEI), liver transplantation, transarterial chemoembolization, and systemic chemotherapy. Of these, only resection, ablation, and transplantation may be associated with curative response.

**Surgical resection.** Due to well preserved hepatic function in residual liver, local tumor resection is the treatment of choice for solitary tumors in non-cirrhotic patients. However, this group represents only 5%–15% of all cases of HCC in Western countries but is more common in Asia due to the higher prevalence of non-cirrhotic chronic hepatitis B infection. Improvements in preoperative selection and surgical technique have led to significant improvements in operative outcomes, which are characterized by surgical mortality rates less than 3%, blood transfusion rates of less than 10%, and 1-, 3-, and 5-year survival rates of 97%, 84%, and 57%, respectively.<sup>5,13</sup> Selecting patients with normal serum bilirubin and the absence of clinically significant portal hypertension (hepatic venous pressure gradient [HVPG] <10 mm Hg) further improves 5-year survival rates to 70%, in comparison to less than 30% among those with elevated bilirubin and clinically significant portal hypertension. The enhanced utilization of intraoperative ultrasound (IOUS) has further improved tumor localization and staging and permits more precise resection with adequate surgical margins. For individuals with baseline impaired hepatic reserve, preoperative portal vein embolization (PVE) may be performed to increase the safety of tumor resection.

Segmental hepatectomy is preferred by some centers due to the concern for microscopic intrahepatic metastasis or de novo tumors, as suggested by rates of recurrent HCC as high as 80%



within 5 years after resection.<sup>14</sup> Tumor size greater than 5 cm in diameter, 3 or more tumors, microvascular invasion, and narrow resection margins appear to represent risk factors for tumor recurrence, although this remains an area of controversy, and inadequate evidence exists to support guidelines on specific tumor number and size limits. In recent genome-wide studies, a gene signature that predicts high risk for tumor-related death from late HCC recurrence was identified and may provide a critically important tool for individualized treatment approaches in these patients.<sup>15</sup> Pre-resection chemoembolization, adjuvant chemotherapy, transarterial radioembolization, and systemic immunotherapy approaches have not demonstrated benefit in preventing recurrence and are not recommended.<sup>16</sup> Only individuals with recurrence stemming from de novo tumor development are likely to respond to repeat resection or salvage transplantation.

**Liver transplantation.** For individuals with decompensated cirrhosis, liver transplantation is the treatment of choice due to its unique properties of both tumor removal and correcting the underlying liver disease. Due to ongoing limitations in organ supply, significant controversy remains in defining the optimal eligibility criteria and the conditions under which individuals not meeting standard requirements may appropriately undergo transplantation. These questions seek to identify an appropriate balance of transplantations performed for HCC in comparison to other indications with optimization of post-transplant outcomes and survival. The present guidelines of the United Network for Organ Sharing (UNOS) are based on Milan criteria in which transplantation in patients with single tumors less than 5 cm in diameter or up to 3 tumors up to 3 cm in diameter each without vascular invasion or extrahepatic spread is associated with 4-year overall and disease-free survival rates of 85% and 92%, respectively, 5-year survival rates of greater than 70%, and recurrence rates lower than 15%.<sup>17,18</sup> More recent evidence from the University of California at San Francisco (UCSF) has led to a proposal for expanded selection criteria that would include single tumors  $\leq 6.5$  cm in diameter or up to 3 tumors, none exceeding 4.5 cm in diameter and a total tumor diameter of 8 cm.<sup>19</sup> In this cohort, 1- and 5-year survival rates were 90% and 75.2%, respectively, similar to outcomes observed in candidates within Milan criteria, although the clinical applicability of these extended criteria is limited due to the use of explant tumor rather than preoperative tumor characteristics.

At present, UNOS assigns liver allocation priority to individuals with HCC within Milan criteria. Based on tumor number and size, Model for End-Stage Liver Disease (MELD) points are assigned scores that provide exception points to those who meet specific parameters. The initial UNOS assignment provided 24 points for single tumors  $< 2$  cm in diameter and 29 points for single tumors 2 cm–5 cm in diameter or up to 3 tumors  $< 3$  cm in diameter each. Due to disproportionate prioritization of patients with HCC in relation to other indications, this was modified to current guidelines of zero exception points for single tumors  $< 2$  cm or  $> 5$  cm in diameter and 22 points for single tumors 2 cm–5 cm in diameter.<sup>20</sup> Additional 3 points are awarded for each 3-month period in which the patient remains on the waiting list, based on an expected increase in pretransplant mortality during this time. A major concern remains for drop-out on the waiting list due to tumor growth, vascular invasion, or liver disease progression, which occurs in as many as 25%–38% of individuals within the first year.<sup>16</sup> Therefore, bridging therapies, such as ablative treatments and chemoembolization to slow tumor progression, have been studied, although the absence of adequate prospective data prevents consensus recommendations on its role pretransplant. Alternatively, living donor liver transplantation (LDLT) represents a particularly attractive option that can be performed in a more timely and controlled fashion, although it is associated with complex ethical considerations. Retrospective trials suggest that LDLT may reduce dropout on the waiting list (414 to 83 days) and have similar 5-year survival rates as high as 68%. However, 3-year HCC recurrence was higher (30% versus 0%), and further prospective studies are required before wider adoption.<sup>21,22</sup> For individuals beyond Milan criteria, “downstaging” the size and number of HCC lesions with ablative therapies or TACE is effective in up to 70% of patients and leads to successful transplantation in nearly half of these cases, although it should only be considered with caution in consultation with experienced transplant centers. Overall, the revised MELD allocation system has resulted in a 6-fold increase in the proportion of transplantation patients with HCC, and larger tumor size (3 cm–5 cm), marked serum AFP elevation ( $\geq 455$  ng/mL), and high MELD score ( $\geq 20$ ) are associated with poorer post-transplant survival.<sup>23</sup>

**Ablative therapies.** Local ablative therapy represents a common strategy for individuals with small localized tumors that are not amenable to resection or do not meet criteria for transplantation, typically due to poor performance status or

impaired liver synthetic function. Strategies, such as percutaneous ethanol injection (PEI), radiofrequency ablation (RFA), cryotherapy, laser therapy, and microwave therapy, have been described, although only PEI and RFA are commonly used in the United States.

Percutaneous ethanol injection involves the slow injection of absolute or 95% ethanol into a tumor under ultrasound guidance, which results in localized coagulative necrosis within the perimeter of the tumor lesion. It is safe, well tolerated, and inexpensive and may achieve necrosis rates of 90%–100% for tumors <2 cm in diameter, although success rates are lower for larger tumors, with rates of 70%–80% for tumors 2 cm–3 cm in diameter and 50% for tumors 3 cm–5 cm in diameter. Among patients with compensated cirrhosis, PEI results in 5-year survival rates of 50%, which are similar to those reported for surgical resection, and is best for individuals with tumors <3 cm in diameter each and with fewer than 3 lesions total.<sup>24,25</sup> This modality is limited by the inability to achieve complete necrosis in larger tumors greater than 3 cm in diameter and the need for multiple sessions to access the entire tumor volume.

Radiofrequency ablation represents a unique thermal technique that can be applied through percutaneous, laparoscopic, or intraoperative approaches and involves the insertion of a single electrode or multiple electrodes that deliver heat to the tumor with corresponding tissue coagulative necrosis. By using a multiple probe technique, precise application of tumor necrosis can be performed over a wider span. As such, current data suggest that while RFA is similarly effective as PEI for small tumors less than 2 cm in diameter, multiple randomized, controlled trials, one systematic review, and one meta-analysis reveal that RFA is clearly associated with superior tumor necrosis rates and improved cancer-free and overall survival at 1, 2, and 3 years.<sup>26,27</sup> Due to these advantages, RFA represents the most common ablative approach to HCC treatment in the United States.

**Transarterial chemoembolization (TACE).** Regional chemoembolization exploits the altered anatomy of HCC in which the hepatic artery provides greater than 90% of the blood supply to tumors. Using intra-arterial administration of chemotherapeutic agents (eg, adriamycin), typically emulsified in lipiodol, with particle embolization via sterile gelatin sponge, steel coils, or polyvinyl alcohol sponge, TACE

represents a common treatment strategy for individuals with large or multifocal tumors that are beyond criteria for resection or percutaneous ablative techniques. Selective embolization of targeted lobar or segmental branches of the hepatic artery results in significant ischemic tumor necrosis. In the absence of commonly accepted protocols, the choice, dose, administration of chemotherapy agent, and approach to embolization remain within the realm of local expertise. Complete tumor responses are rare, and therefore, multiple sessions are typically required.<sup>28</sup> Transarterial chemoembolization has been demonstrated to result in improved survival compared to supportive care, with 2-year survival rates of 63% versus 27%, respectively. Careful patient selection is required, as TACE should not be performed in those with decompensated Child B or C cirrhosis or portal vein invasion. Although self-limited in most cases, postembolization syndrome occurs in as many 50%–90% of cases and is characterized by fever, nausea, vomiting, abdominal pain, ileus, and elevated liver enzymes lasting 24–48 hours following the procedure. Transarterial chemoembolization may rarely be associated with biliary tract necrosis, cholecystitis, pancreatitis, or bile duct injuries.

**Systemic chemotherapy.** The greatest advances in the last 3 years in the management of HCC have been found in the development of new strategies for systemic HCC therapy. Traditional chemotherapy remains a noncurative approach utilized for those individuals with advanced, unresectable HCC who do not meet criteria for ablative therapies or TACE. Hepatocellular carcinoma is notoriously resistant to traditional chemotherapeutic agents or hormonal therapies, and therefore, molecular targeted therapies have emerged as attractive new options for drug therapy. Based on a growing body of literature describing aberrant activation of several signaling pathways critical to regulation and tumorigenesis of HCC, such as epidermal growth factor receptor (EGFR), Raf/mitogen-activated protein (MAP) kinase-extracellular signal-regulated kinase (ERK), phosphoinositol 3-kinase/mammalian target of rapamycin (mTOR), platelet-derived growth factor receptor (PDGFR), vascular endothelial growth factor (VEGF), Wnt, Hedgehog, and hepatocyte growth factor/mesenchymal-epithelial transition factor, new agents targeted at angiogenesis inhibition, telomerase inhibition, and modification of growth-receptor signaling have been identified as potential therapies for HCC.

Sorafenib tosylate (Nexavar, Bayer HealthCare, Wayne, New Jersey) is an oral multitargeted tyrosine kinase inhibitor (TKI) that blocks tumor cell proliferation by inhibition of Raf kinase, MAP kinase kinase (MEK), and ERK pathways and blocks angiogenesis through inhibition of VEGFR-2, VEGFR-3, and PDGFR-beta. In a large, phase 3, randomized, controlled, multicenter trial involving 602 patients who were randomized to oral sorafenib 400 mg daily or placebo daily, nearly all of whom had preserved liver function (95% Child-Pugh A) and advanced disease (37.8% TNM stage 3 and 50.8% TNM stage 4), sorafenib resulted in an improvement in median survival versus placebo (10.7 versus 7.9 months) and a delay in time-to-progression (median 5.5 versus 2.8 months) and demonstrated a hazard ratio for overall survival of 0.69 (95% confidence interval [CI] 0.55–0.87,  $P=$ .0006).<sup>29</sup> Common side

effects included diarrhea (11% versus 2%), hand-foot skin reaction (8% versus 1%), and fatigue (10% versus 15%). A related randomized trial in an Asian cohort of 226 patients demonstrated that in comparison to placebo, sorafenib was associated with a superior disease control rate (defined as a complete or partial response or stable disease maintained for >28 days from first demonstration) of 35% versus 16% (95% CI 28–44), respectively.<sup>30</sup> Sorafenib became the first US Food and Drug Administration-approved agent for HCC in the United States in November 2007, is considered standard of care for individuals with advanced, unresectable HCC who have intact liver synthetic function and are not candidates for ablative therapies or TACE, and should be administered with an oncologist or multidisciplinary HCC team experienced in its use.

## Conclusion

Hepatocellular carcinoma is a rapidly growing cause of cancer and cancer-related death in the United States and represents an important public health priority. Largely due to chronic hepatitis C virus-associated cirrhosis, the incidence of HCC is likely to continue rising within the next decade. Surveillance with abdominal ultrasound and serum AFP every 6–12 months should be performed in all individuals with liver cirrhosis or in high-risk individuals with chronic hepatitis B infection. The diagnosis of HCC is established by the presence of a characteristic vascular pattern on dynamic imaging studies, such as triple-phase helical CT and gadolinium-enhanced MRI, in individuals with cirrhosis with abnormal screening tests. The BCLC system represents a commonly used staging approach due to stage-specific treatment strategies and incorporates assessment of tumor size and characteristics, performance status, and liver synthetic function. Numerous treatment strategies have emerged

within the past decade and have transformed the management of HCC. Liver transplantation remains the treatment of choice for individuals with decompensated cirrhosis and single tumors 2 cm–5 cm in diameter or up to 3 tumors <3 cm in diameter each. Ablative therapies represent preferred treatment for small, localized disease not amenable to resection or transplantation. Transarterial chemoembolization is reserved for noncurative treatment of large or multifocal HCC not amenable to ablative therapy or resection. Sorafenib is a novel oral multikinase inhibitor that represents the first approved agent for HCC based on data demonstrating improved survival in patients with compensated cirrhosis with advanced, unresectable HCC and represents the first of a new generation of molecular targeted therapies that may provide new hope for individuals with liver cancer. A multidisciplinary approach involving hepatologists, oncologists, surgeons, radiologists, and pathologists is essential to optimal management of HCC.

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## Posttest

# Diagnosis and Management of Hepatocellular Carcinoma: 2009 Update

*Please select the 1 best answer by circling the appropriate letter.*

- HCC surveillance is recommend in all of the following patient groups except:
  - Family history of HCC
  - All cirrhotic hepatitis B carriers
  - Asian females  $\geq 40$  years
  - Asian males  $\geq 40$  years
- Tumor size is an insignificant factor in determining the approach to HCC diagnosis. True or False?
  - True
  - False
- The greatest advances in the last three years in the management of HCC have been found in the development of which one of the following?
  - Liver transplant
  - TACE
  - Molecular targeted therapies
  - PEI
- For HCC patients with decompensated cirrhosis, which of the following is considered treatment of choice?
  - Sorafenib
  - Liver transplant
  - TACE
  - RFA
- In the U.S., HCC is associated with cirrhosis in what percentage of patients?
  - 10%-20%
  - 25%-35%
  - 50%-80%
  - 90%-95%

## Evaluation Form

# Diagnosis and Management of Hepatocellular Carcinoma: 2009 Update

*You must complete this evaluation form to receive acknowledgement of participation for this activity.*

*Please answer the following questions by circling the appropriate rating:*

5 = Outstanding    4 = Good    3 = Satisfactory    2 = Fair    1 = Poor

### Extent to Which Program Activities Met the Identified Objectives

- Review the epidemiology and etiology of HCC ..... 5 4 3 2 1
- Describe the latest treatment advances ..... 5 4 3 2 1
- Discuss the latest treatment algorithms for the management of HCC ..... 5 4 3 2 1

### Overall Effectiveness of the Activity

- Was timely and will influence how I practice ..... 5 4 3 2 1
- Will assist me in improving patient care ..... 5 4 3 2 1
- Fulfilled my educational needs ..... 5 4 3 2 1
- Avoided commercial bias or influence ..... 5 4 3 2 1

### Impact of the Activity

- The information presented: *(check all that apply)*
  - Reinforced my current practice/treatment habits
  - Will improve my practice/patient outcomes
  - Provided new ideas or information I expect to use
  - Enhanced my current knowledge base
- Will the information presented cause you to make any changes in your practice?     Yes     No  
If yes, please describe any change(s) you plan to make in your practice as a result of this conference:

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- How committed are you to making these changes?  
(Very committed)    5    4    3    2    1    (Not at all committed)

### Future Activities

- Do you feel future activities on this subject matter are necessary and/or important to your practice?     Yes     No
- Please list any other topics that would be of interest to you for future educational activities:

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### Follow-up

As part of our continuous quality-improvement effort, we conduct post-activity follow-up surveys to assess the impact of our educational interventions on professional practice. Please indicate your willingness to participate in such a survey:

- Yes, I would be interested in participating in a follow-up survey
- No, I'm not interested in participating in a follow-up survey

Additional comments about this activity:

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