PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #348
TREATMENT OPTIONS FOR HEPATOCELLULAR CARCINOMA
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Hepatocellular carcinoma (HCC) is the third most common cause of cancer-related mortality worldwide (1). This *Fast Fact* provides an overview of staging and treatment options for generalist and palliative care clinicians who are often asked to navigate complicated decision making in HCC patients.

HCC Staging:

Treatment Goal	BCLC[a] Stage at Diagnosis	Treatment Options
Curative	0: single nodule < 2 cm A: 1-3 nodules <3 cm	Surgical resection or orthotopic liver transplantation
Life prolongation	B: >3 nodules with an ECOG PS[b] of 0 C: portal invasion, nodal involvement or metastasis with ECOG PS of 1-2	Localized arterially directed therapy or Systemic medical therapy
Comfort	D: BCLC Stage C with ECOG PS >2	Hospice eligible

[a]Barcelona Clinic Liver Cancer; [b]Eastern Cooperative Oncology Group Performance Status

Prognosis and Quality of Life (QoL): Only 10-15% of HCC patients have curative options at the time of diagnosis (2). This clinical factor plus the high prevalence of cirrhosis as a comorbidity contributes to a 5-year survival rate of only 10% (3). BCLC staging is an important prognostic factor. Whereas, the one-year survival rate is 77-83% with treatment (33% without treatment) when HCC is localized to the liver; the one-year survival of metastatic disease is only 15% (3). HCC patients often suffer from pain, jaundice, anorexia, and depression as well as ascites, fatigue and edema from coexisting cirrhosis (4). This debilitating symptom burden leads to a diminished health-related quality of life (QoL) (4).

Localized, Arterially Directed Therapy: While normal liver tissue is perfused by the hepatic artery and portal vein, HCC is almost exclusively supplied by the hepatic artery (5). This has led to the development of arterially directed techniques to block hepatic tumor perfusion via the localized delivery of chemotherapy or radiotherapy. These procedures are performed and clinically monitored by specialized interventional radiologists. They are reserved for patients with unresectable HCC who have preserved liver function, an ECOG PS of 0-2, and no evidence of extra-hepatic disease (6). Relative contraindications include infection, leukopenia, renal insufficiency, decompensated heart failure, hepatic encephalopathy, and biliary obstruction. The goal of this therapy is to improve QoL, prolong survival, and in some cases, downstage the tumor in hopes of making the mass surgically resectable

Commonly Used Localized, Arterially Directed Therapies

- Conventional Transarterial Chemoembolization (cTACE): cTACE uses a combination of cytotoxic chemotherapy (typically cisplatin and doxorubicin) and an oily embolic material called lipiodol. This substance is injected into the hepatic arteries directly supplying the liver mass (7).
- Drug Eluting Bead Transarterial Chemoembolization (DEB-TACE): DEB-TACE differs from cTACE by using drug eluting microspheres instead of lipiodol to locally administer chemotherapy which are associated with increased tumor retention and less systemic toxicity (8).
- Radioembolization with Yttrium-90 (Y-90): Microspheres made of glass or resin are tagged with a radioactive material, most commonly Y-90, and delivered to the malignant liver mass via tumor feeding arteries to induce tumor cell death (9).

Treatment Effect on Symptoms and Quality of Life: Studies have demonstrated survival benefits as well as improvements in patient-reported outcomes including QoL, pain, function, and emotional well-being with cTACE, DEB-TACE, and Y-90 in patients with BCLC B or C disease (10-12). Compared to cTACE, Y-90 was associated with less nervousness, less side effects, less hospitalizations, and an improved QoL (12). However, Y-90 is more expensive with an approximate cost of $31,000 to $48,000 comparted to $17,000 for cTACE (13). In many centers, cTACE is more commonly utilized, but controversy remains regarding the optimal localized, arterially directed therapy.

Treatment Complications: Postembolization syndrome characterized by a resolving, 3-day course of pain, nausea, and vomiting can occur with cTACE and DEB-TACE. A short course of IV opioids, corticosteroids, 5HT3 receptor antagonists, and/or ketorolac in a hospital setting have been described as an effective way to manage this syndrome (14). In more rare circumstances, chemoembolization can lead to vascular injury, hepatic failure, abscess formation, tumor rupture, ulcer formation, and biliary duct injury (15). Y-90 is not associated with postembolization syndrome and severe complications appear to be rarer. As a result, hospitalization is often unnecessary (6,16).

Progression After Localized Therapy: Many with advanced HCC are faced with the complicated decision of whether to pursue systemic targeted therapy, most usually oral sorafenib. Although sorafenib is associated with a significant improvement in median survival (10.7 months vs 7.9 months with placebo) for patients with BCLC Stage C (17,18), several trade-offs need to be considered. These trade-offs include a substantial risk for diarrhea, nausea, liver dysfunction, and cytopenia. It is also associated with increased health care costs and clinic visits which can be barriers for hospice initiation. Hence, QoL, not just prognostic, concerns need to be elicited before deciding about sorafenib. For HCC patients with life prolonging goals who progress through sorafenib therapy, the FDA approved the use of nivolumab based on phase 1 and 2 data showing a 18.2% response rate (19).

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