Advances in HCC Treatment

Hepatocellular carcinoma (HCC) is the third-leading cause of cancer-related deaths worldwide. Incidence rates of HCC are on the rise in the United States and worldwide, where the main risk factors are chronic hepatitis C, alcoholic cirrhosis and non-alcoholic steatohepatitis. Advances in curative options, including liver transplant, surgical resection and ablation, have improved survival for patients with HCC, as have advances in other locoregional treatments such as transarterial chemoembolization (TACE) and radiation therapy.

Specialists at the Massachusetts General Hospital Liver Center work closely with colleagues in the Mass General Cancer Center, Mass General Transplant Center and Mass General Interventional Radiology to design a comprehensive, individualized treatment plan for your patient. Our liver disease programs combine extensive clinical expertise with advanced medical technologies and leading research to offer every patient the highest quality therapies personalized to their condition.

We hope this issue of Liver Center News, the Mass General Liver Center e-newsletter, provides insight into our clinic and our recommendations for the screening and treatment of HCC.

Kathleen E. Corey, MD, MPH
Director, Mass General Fatty Liver Clinic

James F. Markmann, MD, PhD
Chief, Division of Transplantation
Surgical Director, Liver, Pancreas and Islet Transplant
Program, Mass General Transplant Center

Andrew X. Zhu, MD, PhD
Director of Liver Cancer Research
Mass General Cancer Center

To refer a patient to the Liver Center, contact Nicole Demarzo at 855-644-3322 or ndemarzo@partners.org

Transplantation Options for Patients with Unresectable HCC

An important advance in liver transplantation for patients with unresectable HCC was the adoption of Milan criteria to identify those who are expected to achieve excellent recurrence-free survival post-transplantation.

These criteria, defined by Mazzaferro et al in 1996, restrict transplant priority to those with:

- Single lesions ≥ 2 cm and ≤ 5 cm
- Up to three lesions ≥ 1 cm and ≤ 3 cm each

Adherence to these criteria yields survival rates of 75% at five years. Recent accumulating data suggest that patients with lesions even beyond the Milan criteria can achieve excellent outcomes post-transplantation. Most widely recognized are the University of California San Francisco (UCSF) criteria, which experience outcomes equivalent to Milan:

- Single lesions ≤ 8 cm
- Up to three lesions with a max diameter of 4.5 cm (and max cumulative diameter of 8 cm)

Current national United Network for Organ Sharing allocation guidelines do not provide allocation priority to patients meeting these expanded criteria. However, at Mass General, we have adopted the position that patients with lesions beyond Milan, but meeting UCSF criteria, who remain stable for a period post-locoregional ablative therapy, will be considered acceptable for transplantation. Since allocation priority is not awarded to such candidates, we rely on live donor transplantation and use of expanded criteria donors. This approach provides the only option for curative therapy for patients with a tumor burden exceeding the Milan criteria; our preliminary experience with the practice has been very encouraging.

Algorithm for Evaluation and Management of Liver Lesions

To refer a patient to the Liver Center, contact Nicole Demarzo at 855-644-3322 or ndemarzo@partners.org
Evaluation and Management of Liver Lesions:

A systemic method of evaluating patients found to have liver lesions on imaging scans.

Frequently Asked Questions About Cirrhosis and HCC

1. How often should patients with cirrhosis be screened for HCC?
2. Can HCC occur in patients without cirrhosis?
3. Can patients with cirrhosis and HCC still receive a liver transplant?
4. What treatment options does Mass General offer to patients with HCC beyond the standard therapies?

Mass General HCC Team

The HCC team at Mass General comprises leading physicians within the fields of imaging, pathology, surgery and oncology who provide comprehensive care to patients with HCC.
Conferences are held each week to review patient cases and provide a multispecialty approach to treatment recommendations. Learn more about the HCC team.

James Markmann, MD, PhD, Chief, Division of Transplantation

Clinical Trials of Systemic Therapy in HCC

**Phase II Trial of Sorafenib in Combination with Modified FOLFOX in Patients With Advanced Hepatocellular Carcinoma**
The goal of this trial is to test the effectiveness of an investigational combination of drugs to learn whether the drug combination works in treating advanced HCC.

Pl: Andrew X. Zhu, MD, PhD
Key Eligibility: Child Pugh score of A; No prior systemic therapy for HCC

**Dose Escalation Study of OMP-54F28 in Combination With Sorafenib in Patients with Hepatocellular Cancer**
This is an open-label Phase 1b dose-escalation study to assess the safety, tolerability and PK of OMP-54F28 when combined with sorafenib.

Pl: Andrew X. Zhu, MD, PhD
Key Eligibility: Child Pugh score of A; No prior systemic therapy

**A Phase 1 Study of LY2875358 in Patients with Advanced Cancer**
The objective of this study is to determine a recommended Phase 2 dose range of LY2875358 that may be safely administered to participants with advanced cancer.

Pl: Andrew X. Zhu, MD, PhD
Key Eligibility: Tumor c-MET overexpression; ≥ 1 prior systemic therapy for HCC

**A Randomized Three Arm Phase II Study of (1) Everolimus, (2) Estrogen Deprivation Therapy (EDT) With Leuprolide + Letrozole and (3) Everolimus + EDT in Patients with Unresectable Fibrolamellar Hepatocellular Carcinoma (FLL-HCC)**
The goal of this study is to understand the effects that three drugs—leuprolide, leuprolide and everolimus—will have on cancer.

Pl: Robert Mayer, MD
Key Eligibility: Tumor c-MET overexpression; ≥ 1 prior systemic therapy for HCC

To refer a patient to the Liver Center, contact Nicole Demarzo at 855-644-3322 or ndemarzo@partners.org
Fibroscan®, also called transient elastography, is now available at Mass General. Fibroscan is a noninvasive method to assess for liver stiffness or scarring and can be performed during a 30-minute office visit. Fibroscan is currently covered by Medicare, and for others, carries an out-of-pocket cost of $200. For more information, or to schedule a Fibroscan, please contact Nicole Demarzo at 855-644-3322.