

Hepatocellular Carcinoma Update

Issue 1, 2018 (Video Program)

CME Information

TARGET AUDIENCE

This activity is intended for medical oncologists, hematologist-oncologists and other healthcare providers involved in the treatment of hepatocellular carcinoma (HCC).

OVERVIEW OF ACTIVITY

HCC, the most common form of liver cancer, is the third leading cause of cancer-related deaths worldwide. The rising incidence, multiple etiologies, genetic heterogeneity and concurrent chronic liver disease make the selection of treatment for this cancer challenging. In addition, HCC is often diagnosed in the advanced stage and is associated with a poor prognosis. However, recent breakthroughs in understanding the etiology and pathogenesis have led to the advent of new treatment modalities and investigational therapies. In order to offer optimal patient care, the practicing oncologist must be well informed of these advances. To bridge the gap between research and patient care, this issue of *Hepatocellular Carcinoma Update* uses one-on-one discussions with leading oncology investigators. By providing access to the latest research developments and expert perspectives on the disease, this CME program will assist medical oncologists and select gastroenterology specialists in the formulation of up-to-date clinical management strategies for patients with HCC.

LEARNING OBJECTIVES

- Consider patient age, performance status, liver function and other clinical and logistical factors in the up-front management of newly diagnosed unresectable or metastatic HCC.
- Appreciate the FDA approval of regorafenib for patients who have experienced treatment failure with sorafenib, and discern how regorafenib can be optimally integrated into clinical management.
- Appraise recent Phase III data with lenvatinib, and consider the clinical role of this agent in the management of previously untreated unresectable HCC.
- Recall available efficacy and safety data with cabozantinib, and consider the potential clinical role of this agent for patients who experience disease progression on sorafenib.
- Understand the scientific rationale for and recall available clinical trial data with approved and investigational checkpoint inhibitors in the treatment of HCC.
- Evaluate emerging Phase III data with ramucirumab in patients with advanced HCC and elevated alpha-fetoprotein who have experienced disease progression after treatment with sorafenib.

ACCREDITATION STATEMENT

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AMERICAN BOARD OF INTERNAL MEDICINE (ABIM) — MAINTENANCE OF CERTIFICATION (MOC)

Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 2.5 Medical Knowledge MOC points in the American Board of Internal Medicine's (ABIM) Maintenance of Certification (MOC) program. Participants will earn MOC points equivalent to the amount of CME credits claimed for the activity. It is the CME activity provider's responsibility to submit participant completion information to ACCME for the purpose of granting ABIM MOC credit.

Please note, this program has been specifically designed for the following ABIM specialty: **medical oncology**.

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FACULTY — The following faculty (and their spouses/partners) reported relevant conflicts of interest, which have been resolved through a conflict of interest resolution process:

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Hardware/Software Requirements:

A high-speed Internet connection
A monitor set to 1280 x 1024 pixels or more
Internet Explorer 11 or later, Firefox 56 or later, Chrome 61 or later, Safari 11 or later, Opera 48 or later
Adobe Flash Player 27 plug-in or later
Adobe Acrobat Reader
(Optional) Sound card and speakers for audio

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Select Publications

Abou-Alfa GK et al. **Cabozantinib (C) versus placebo (P) in patients (pts) with advanced hepatocellular carcinoma (HCC) who have received prior sorafenib: Results from the randomized phase III CELESTIAL trial.** Gastrointestinal Cancers Symposium 2018;[Abstract 207](#).

Abou-Alfa GK et al. **Cabozantinib in patients with advanced and progressing hepatocellular carcinoma.** *N Engl J Med* 2018;379(1):54-63.

A randomized, multi-center phase III study of nivolumab versus sorafenib as first-line treatment in patients with advanced hepatocellular carcinoma (CheckMate 459: Checkpoint pathway and nivolumab clinical trial evaluation 459). [NCT02576509](#)

A randomized, open-label, multi-center phase III study of durvalumab and tremelimumab as first-line treatment in patients with unresectable hepatocellular carcinoma. [NCT03298451](#)

Bruix J et al. **Regorafenib for patients with hepatocellular carcinoma who progressed on sorafenib treatment (RESORCE): A randomised, double-blind, placebo-controlled, phase 3 trial.** *Lancet* 2017;389(10064):56-66.

Bruix J et al. **Updated overall survival (OS) analysis from the international, phase 3, randomized, placebo-controlled RESORCE trial of regorafenib for patients with hepatocellular carcinoma (HCC) who progressed on sorafenib treatment.** *Proc ESMO World Congress on Gastrointestinal Cancer* 2017;[Abstract O-009](#).

Cheng AL et al. **Efficacy and safety of sorafenib in patients in the Asia-Pacific region with advanced hepatocellular carcinoma: A phase III randomised, double-blind, placebo-controlled trial.** *Lancet Oncol* 2009;10(1):25-34.

Chow PKH et al. **SIRveNIB: Selective internal radiation therapy versus sorafenib in Asia-Pacific patients with hepatocellular carcinoma.** *J Clin Oncol* 2018;36(19):1913-21.

El-Khoueiry AB et al. **Nivolumab in patients with advanced hepatocellular carcinoma (CheckMate 040): An open-label, non-comparative, phase 1/2 dose escalation and expansion trial.** *Lancet* 2017;389(10088):2492-502.

Frenette CT. **The role of regorafenib in hepatocellular carcinoma.** *Clin Adv Hematol Oncol* 2017;15(2):121-3.

Ikeda M et al. **A phase 1b trial of lenvatinib (LEN) plus pembrolizumab (PEM) in patients (pts) with unresectable hepatocellular carcinoma (uHCC).** *Proc ASCO* 2018;[Abstract 4076](#).

Kudo M et al. **Lenvatinib versus sorafenib in first-line treatment of patients with unresectable hepatocellular carcinoma: A randomised phase 3 non-inferiority trial.** *Lancet* 2018;391(10126):1163-73.

Lemery S et al. **First FDA approval agnostic of cancer site — When a biomarker defines the indication.** *N Engl J Med* 2017;377(15):1409-12.

Lencioni R et al. **Sorafenib or placebo plus TACE with doxorubicin-eluting beads for intermediate stage HCC: The SPACE trial.** *J Hepatol* 2016;64(5):1090-8.

Llovet JM et al; SHARP Investigators Study Group. **Sorafenib in advanced hepatocellular carcinoma.** *N Engl J Med* 2008;359(4):378-90.

Sangro B et al. **A randomized, multicenter, phase 3 study of nivolumab vs sorafenib as first-line treatment in patients (pts) with advanced hepatocellular carcinoma (HCC): CheckMate-459.** *Proc ASCO* 2016;[Abstract TPS4147](#).

Vilgrain V et al; SARAH Trial Group. **Efficacy and safety of selective internal radiotherapy with yttrium-90 resin microspheres compared with sorafenib in locally advanced and inoperable hepatocellular carcinoma (SARAH): An open-label randomised controlled phase 3 trial.** *Lancet Oncol* 2017;18(12):1624-36.

Zhu AX et al. **Pembrolizumab (pembro) in patients with advanced hepatocellular carcinoma (HCC): KEYNOTE-224 update.** *Proc ASCO* 2018;[Abstract 4020](#).

Zhu AX et al. **REACH-2: A randomized, double-blind, placebo-controlled phase 3 study of ramucirumab versus placebo as second-line treatment in patients with advanced hepatocellular carcinoma (HCC) and elevated baseline alpha-fetoprotein (AFP) following first-line sorafenib.** *Proc ASCO* 2018;[Abstract 4003](#).

Zhu AX et al; REACH Trial Investigators. **Ramucirumab versus placebo as second-line treatment in patients with advanced hepatocellular carcinoma following first-line therapy with sorafenib (REACH): A randomised, double-blind, multicentre, phase 3 trial.** *Lancet Oncol* 2015;16(7):859-70.