Oncology Today with Dr Neil Love: Gastrointestinal Cancers Edition 2019 — Hepatocellular Carcinoma

Audio Program

CME Information

TARGET AUDIENCE

This activity is intended for medical oncologists, hematologists-oncologists, hematology-oncology fellows and other healthcare providers involved in the treatment of gastrointestinal cancers.

OVERVIEW OF ACTIVITY

Hepatocellular carcinoma (HCC), the most common form of liver cancer, is the fourth leading cause of cancer-related death worldwide. A rising incidence, multiple etiologies, genetic heterogeneity and concurrent chronic liver disease make the selection of treatment for HCC challenging, and the disease is often diagnosed in the advanced stage, at which it is associated with poor prognosis. 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 *Oncology Today with Dr Neil Love* focusing on HCC features a discussion with 2 leading gastrointestinal oncology investigators. By providing access to the latest research developments and expert perspectives on the disease, this CME activity assists medical oncologists and select gastroenterology specialists in the formulation of up-to-date clinical management strategies.

LEARNING OBJECTIVES

- Consider patient age, performance status, liver function and other clinical and logistical factors in the up-front and subsequent management of unresectable or metastatic HCC.
- Appraise recent Phase III data with lenvatinib, and consider its clinical role in the care of patients with previously untreated unresectable HCC.
- Appreciate the recent FDA approval of cabozantinib for patients who have previously received sorafenib, and consider how this agent can be optimally integrated into therapy for these individuals.
- Understand the biologic rationale for immune checkpoint inhibition in the treatment of HCC, and recall available clinical data with approved and investigational checkpoint inhibitors.
- Recognize immune-related adverse events and other common side effects associated with approved and developmental immune checkpoint inhibitors, and offer supportive management strategies to minimize and manage these toxicities.
- Evaluate the latest Phase III data with ramucirumab for patients with advanced HCC and elevated alpha-fetoprotein who previously received sorafenib.

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Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 1.5 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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This activity is supported by an educational grant from Lilly.

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

Last review date: February 2019

Expiration date: February 2020

Select Publications

A phase III, open-label, randomized study of atezolizumab in combination with bevacizumab compared with sorafenib in patients with untreated locally advanced or metastatic hepatocellular carcinoma. NCT03434379

Abou-Alfa GK et al. **A randomized, multicenter phase 3 study of durvalumab (D) and tremelimumab (T) as first-line treatment in patients with unresectable hepatocellular carcinoma (HCC): HIMALAYA study.** *Proc ASCO* 2018;**Abstract TPS4144**.

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.

Brar G et al. **Hepatocellular carcinoma (HCC) survival by etiology: A SEER-Medicare database analysis.** Gastrointestinal Cancers Symposium 2019;**Abstract 201**.

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**.

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.

Finn R et al. **Ramucirumab (RAM) as second-line treatment in patients with advanced hepatocellular carcinoma (HCC) and elevated baseline α-fetoprotein (AFP): An analysis of AFP kinetics in the phase III REACH-2 study.** Gastrointestinal Cancers Symposium 2019;**Abstract 326**.

Finn RS et al. **Outcomes of sequential treatment with sorafenib followed by regorafenib for HCC: Additional analyses from the phase III RESORCE trial.** *J Hepatol* 2018;69(2):353-8.

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**.

Kaseb AO et al. **Randomized, open-label, perioperative phase II study evaluating nivolumab alone versus nivolumab plus ipilimumab in patients with resectable HCC.** Gastrointestinal Cancers Symposium 2019;**Abstract 185**.

Kudo M et al. **Ramucirumab as second-line treatment in patients with advanced hepatocellular carcinoma (HCC) and elevated alpha-fetoprotein (AFP) following first-line sorafenib: Pooled efficacy and safety in Japanese patients across two global randomized phase III studies (REACH-2 and REACH).** Gastrointestinal Cancers Symposium 2019;**Abstract 320**.

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.

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

Okusaka T et al. **Safety and efficacy of lenvatinib by starting dose (8 mg or 12 mg) based on body weight in patients with unresectable hepatocellular carcinoma in REFLECT.** Gastrointestinal Cancers Symposium 2019;**Abstract 316**.

Personeni N et al. **Liver injury by immune checkpoint inhibitors in patients with hepatocellular carcinoma.** Gastrointestinal Cancers Symposium 2019;**Abstract 341**.

Thota R et al. **Characterization of the tumor mutation burden in hepatobiliary tumors.** Gastrointestinal Cancers Symposium 2019;**Abstract 295**.

Vilgrain V et al. **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**.

Select Publications

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; KEYNOTE-224 Investigators. **Pembrolizumab in patients with advanced hepatocellular carcinoma previously treated with sorafenib (KEYNOTE-224): A non-randomised, open-label phase 2 trial.** *Lancet Oncol* 2018;19(7):940-52.

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.