Meet The Professors

Clinical Investigator Perspectives on Key Questions and Emerging Research in the Management of Colorectal, Gastric and Hepatocellular Cancer

CME Information

TARGET AUDIENCE

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

OVERVIEW OF ACTIVITY

Given the prevalent nature of the disease, extensive resources are allocated to colorectal cancer research and education. Interestingly, however, although individually less frequently encountered, the collection of other noncolorectal GI cancers accounts for more per annum cancer-related deaths than those attributed to tumors of the colon and rectum combined. Among this collection of distinct tumor types, a few areas in particular — namely gastric/gastroesophageal and hepatocellular cancer — have witnessed several recent advances that have altered or have the potential to drastically alter current treatment considerations and approaches.

These video proceedings from a CME symposium held during the 2019 Gastrointestinal Cancers Symposium feature discussions with leading researchers with an expertise in GI cancers regarding actual cases from their practices and the published data that drive clinical decision-making for patients in those and diverse other situations. By providing information on the latest research developments and their potential application to routine practice, this activity is designed to assist medical oncologists, hematology-oncology fellows and other healthcare providers with the formulation of up-to-date clinical management strategies.

LEARNING OBJECTIVES

- Develop a long-term care plan for patients diagnosed with metastatic colorectal cancer, considering biomarker profile, tumor location, prior systemic therapy, symptomatology, performance status and personal goals of treatment.
- Use HER2 status, PD-L1 combined positive score, clinical factors and patient preferences to optimize the selection and sequence of systemic therapy for locally advanced or metastatic gastric/gastroesophageal cancer.
- Review recent therapeutic advances and related FDA authorizations for patients with newly diagnosed and relapsed/refractory advanced hepatocellular carcinoma, and integrate this information, as appropriate, into routine clinical practice.
- Recall the biologic rationale for, published clinical trial data with and ongoing research evaluating the use of immune checkpoint inhibitors alone or in combination with chemotherapy, targeted agents or other immunotherapies for colorectal, esophageal, gastric/gastroesophageal and hepatocellular cancer, and identify patients who may be eligible for these strategies in or outside of a protocol setting.
- Appreciate available Phase III data with and consider the potential clinical roles of novel agents (eg, cabozantinib, ramucirumab, TAS-102) that may soon provide additional treatment options to patients with diseases beyond those for which those agents were initially indicated.
- Design and implement a plan of care to recognize and manage side effects and toxicities associated with novel and recently approved systemic therapies for locally advanced or metastatic colorectal, gastric and hepatocellular cancer to support quality of life and continuation of therapy.
- Recall available and emerging data with other investigational agents currently in clinical testing for colorectal, gastric/gastroesophageal and hepatocellular cancer, and, where applicable, refer eligible patients for trial participation or other expanded access programs.

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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

Gastric and Gastroesophageal Cancer

Fuchs CS et al. **Safety and efficacy of pembrolizumab monotherapy in patients with previously treated advanced gastric and gastroesophageal junction cancer: Phase 2 clinical KEYNOTE-059 trial.** *JAMA Oncol* 2018;4(5):e180013.

Fuchs CS et al. **KEYNOTE-059 cohort 1: Efficacy and safety of pembrolizumab (pembro) monotherapy in patients with previously treated advanced gastric cancer.** *Proc ASCO* 2017;**Abstract 4003**.

Ilson DH et al. **Efficacy and safety of trifluridine/tipiracil (FTD/TPI) in patients (pts) with metastatic gastric cancer (mGC) with or without prior gastrectomy: Results from a phase III study (TAGS).** Gastrointestinal Cancers Symposium 2019;**Abstract 3**.

Janjigian YY et al. **CheckMate-032 study: Efficacy and safety of nivolumab and nivolumab plus ipilimumab in patients with metastatic esophagogastric cancer.** *J Clin Oncol* 2018;36(28):2836-44.

Kang YK et al. **Nivolumab in patients with advanced gastric or gastro-oesophageal junction cancer refractory to, or intolerant of, at least two previous chemotherapy regimens (ONO-4538-12, ATTRACTION-2): A randomised, double-blind, placebo-controlled, phase 3 trial.** *Lancet* 2017;390(10111):2461-71.

Kojima T et al. **Pembrolizumab versus chemotherapy as second-line therapy for advanced esophageal cancer: Phase III KEYNOTE-181 study.** Gastrointestinal Cancers Symposium 2019;**Abstract 2**.

Pavlakis N et al. **Regorafenib for the treatment of advanced gastric cancer (INTEGRATE): A multinational placebo-controlled phase II trial.** *J Clin Oncol* 2016;34(23):2728-35.

Shitara K et al. **Pembrolizumab versus paclitaxel for previously treated, advanced gastric or gastro-oesophageal junction cancer (KEYNOTE-061): A randomised, open-label, controlled, phase 3 trial.** *Lancet* 2018;392(10142):123-33.

Shitara K et al. **Trifluridine/tipiracil versus placebo in patients with heavily pretreated metastatic gastric cancer (TAGS): A randomised, double-blind, placebo-controlled, phase 3 trial.** *Lancet Oncol* 2018;19(11):1437-48.

Tabernero J et al. **Overall survival results from a phase III trial of trifluridine/tipiracil versus placebo in patients with metastatic gastric cancer refractory to standard therapies (TAGS).** *Proc ESMO World Congress on Gastrointestinal Cancer* 2018;**Abstract LBA-002**.

Hepatocellular Carcinoma

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

Abou-Alfa G et al. **Quality-adjusted life years assessment using cabozantinib for patients with advanced hepatocellular carcinoma (aHCC) in the CELESTIAL trial.** Gastrointestinal Cancers Symposium 2018;**Abstract 207**.

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.

Cheng AL et al. **Phase III trial of lenvatinib (LEN) vs sorafenib (SOR) in first-line treatment of patients (pts) with unresectable hepatocellular carcinoma (uHCC).** *Proc ASCO* 2017;**Abstract 4001**.

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 RS et al. **A multicenter, open-label, phase 3 trial to compare the efficacy and safety of lenvatinib (E7080) versus sorafenib in first-line treatment of subjects with unresectable hepatocellular carcinoma.** *Proc ASCO* 2014;**Abstract TPS4153**.

Ikeda K et al. **Phase 2 study of lenvatinib in patients with advanced hepatocellular carcinoma.** *J Gastroenterol* 2017;52(4):512-9.

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**.

Kelley RK et al. **Phase I/II study of durvalumab and tremelimumab in patients with unresectable hepatocellular carcinoma (HCC): Phase I safety and efficacy analyses.** *Proc ASCO* 2017;**Abstract 4073**.

Kudo M et al. **Analysis of survival and objective response (OR) in patients with hepatocellular carcinoma in a phase III study of lenvatinib (REFLECT).** Gastrointestinal Cancers Symposium 2019;**Abstract 186**.

Kudo M et al. **Checkmate-040: Nivolumab (NIVO) in patients (pts) with advanced hepatocellular carcinoma (aHCC) and Child-Pugh B (CPB) status.** Gastrointestinal Cancers Symposium 2019;**Abstract 327**.

Select Publications

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. **Sorafenib in advanced hepatocellular carcinoma.** *N Engl J Med* 2008;359(4):378-90.

Pishvaian MJ et al. **Updated safety and clinical activity results from a phase Ib study of atezolizumab + bevacizumab in hepatocellular carcinoma (HCC).** *Proc ESMO* 2018;**Abstract LBA26**.

Stjepanovic N, Capdevila J. **Multikinase inhibitors in the treatment of thyroid cancer: Specific role of lenvatinib.** *Biologics* 2014;8:129-39.

Zhu AX et al. **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-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**.

Colorectal Cancer

Bekaii-Saab TS et al. **Regorafenib dose optimization study (ReDOS): Randomized phase II trial to evaluate escalating dosing strategy and pre-emptive topical steroids for regorafenib in refractory metastatic colorectal cancer (mCRC) — an ACCRU Network study.** *Proc ESMO* 2018;**Abstract O-014**.

Bekaii-Saab TS et al. **Regorafenib dose optimization study (ReDOS): Randomized phase II trial to evaluate dosing strategies for regorafenib in refractory metastatic CRC (mCRC) — an ACCRU Network study.** Gastrointestinal Cancers Symposium 2018;**Abstract 611**.

Chen EX et al. **CCTG CO.26 trial: A phase II randomized study of durvalumab (D) plus tremelimumab (T) and best supportive care (BSC) versus BSC alone in patients (pts) with advanced refractory colorectal carcinoma (rCRC).** Gastrointestinal Cancers Symposium 2019;**Abstract 481**.

Diaz LA et al. **Pembrolizumab therapy for microsatellite instability high (MSI-H) CRC and non-CRC.** *Proc ASCO* 2017;**Abstract 3071**.

Falcone A et al. **Safety and efficacy of trifluridine/tipiracil in previously treated metastatic colorectal cancer (mCRC): Preliminary results from the phase IIIb, international, open-label, early-access PRECONNECT study.** *Proc ESMO World Congress on Gastrointestinal Cancer* 2018;**Abstract O-013**.

Kopetz S et al. **Updated results of the BEACON CRC safety lead-in: Encorafenib (ENCO) + binimetinib (BINI) + cetuximab (CETUX) for BRAFV600E-mutant metastatic colorectal cancer (mCRC).** Gastrointestinal Cancers Symposium 2019;**Abstract 688**.

Kopetz S et al. **Randomized trial of irinotecan and cetuximab with or without vemurafenib in BRAF-mutant metastatic colorectal cancer (SWOG S1406).** *Proc ASCO* 2017;**Abstract 3505**.

Le DT et al. **PD-1 blockade in tumors with mismatch-repair deficiency.** *N Engl J Med* 2015;372(26):2509-20.

Overman MJ et al. **Durable clinical benefit with nivolumab plus ipilimumab in DNA mismatch repair-deficient/microsatellite instability-high metastatic colorectal cancer.** *J Clin Oncol* 2018;36(8):773-9.

Overman MJ et al. **Nivolumab in patients with metastatic DNA mismatch repair-deficient or microsatellite instability-high colorectal cancer (CheckMate 142): An open-label, multicentre, phase 2 study.** *Lancet Oncol* 2017;18(9):1182-91.

Sartore-Bianchi A et al. **Dual-targeted therapy with trastuzumab and lapatinib in treatment-refractory, KRAS codon 12/13 wild-type, HER2-positive metastatic colorectal cancer (HERACLES): A proof-of-concept, multicentre, open-label, phase 2 trial.** *Lancet Oncol* 2016;17(6):738-46.

Shitara K et al. **Reverce: Randomized phase II study of regorafenib followed by cetuximab versus the reverse sequence for metastatic colorectal cancer patients previously treated with fluoropyrimidine, oxaliplatin, and irinotecan.** Gastrointestinal Cancers Symposium 2018;**Abstract 557**.

Van Cutsem E et al. **BEACON CRC study safety lead-in: Assessment of the BRAF inhibitor encorafenib + MEK inhibitor binimetinib + anti-epidermal growth factor receptor antibody cetuximab for BRAFV600E metastatic colorectal cancer.** *Proc ESMO World Congress on Gastrointestinal Cancer* 2018;**Abstract O-027**.

Xu J et al. **Results of a randomized, double-blind, placebo-controlled, phase III trial of trifluridine/tipiracil (TAS-102) monotherapy in asian patients with previously treated metastatic colorectal cancer: The TERRA study.** *J Clin Oncol* 2018;36(4):350-8.