

An Evening with the Investigators

Perspectives on Key Questions and Emerging Research in the Management of Gastrointestinal Cancers

CME Information

TARGET AUDIENCE

This program is intended for medical oncologists, hematology-oncology fellows and other allied healthcare professionals 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, pancreatic 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 2018 ASCO Annual Meeting 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

- Review recent data on therapeutic advances and changing practice standards in colorectal and noncolorectal GI cancers, and integrate this information, as appropriate, into current clinical care.
- Develop a long-term care plan for individuals diagnosed with metastatic colorectal cancer, considering biomarker profile, tumor location, prior systemic therapy, symptomatology, performance status (PS) 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.
- Consider age, PS and other clinical and logistical factors in the selection of systemic therapy for patients with localized, locally advanced or metastatic pancreatic adenocarcinoma.
- Communicate the benefits and risks of available and emerging systemic interventions to patients with locally advanced or metastatic hepatocellular carcinoma.
- Appraise the rationale for and clinical data with commercially available and developmental immune checkpoint inhibitors in the treatment of GI cancers.
- Recall the design of ongoing clinical trials evaluating novel investigational agents in GI cancers, and counsel appropriately selected patients about availability and participation.

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Successful completion of this CME activity, which includes participation in the evaluation component, enables the participant to earn up to 2.75 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

Module 1: Gastric Cancer

Al-Batran SE et al. **FAST: An international, multicenter, randomized, phase II trial of epirubicin, oxaliplatin, and capecitabine (EOX) with or without IMAB362, a first-in-class anti-CLDN18.2 antibody, as first-line therapy in patients with advanced CLDN18.2+ gastric and gastroesophageal junction (GEJ) adenocarcinoma.** ASCO 2016;Abstract LBA4001.

Bando H et al. **A multicenter phase II study of TAS-102 monotherapy in patients with pre-treated advanced gastric cancer (EPOC1201).** *Eur J Cancer* 2016;62:46-53.

Fuchs CS et al. **Pembrolizumab (pembro) vs paclitaxel (PTX) for previously treated advanced gastric or gastroesophageal junction (G/GEJ) cancer: Phase 3 KEYNOTE-061 trial.** ASCO 2018;Abstract 4062.

Fuchs CS et al. **RAINFALL: A randomized, double-blind, placebo-controlled phase III study of cisplatin (Cis) plus capecitabine (Cape) or 5FU with or without ramucirumab (RAM) as first-line therapy in patients with metastatic gastric or gastroesophageal junction (G-GEJ) adenocarcinoma.** Gastrointestinal Cancers Symposium 2018;Abstract 5.

Fuchs CS et al. **Ramucirumab monotherapy for previously treated advanced gastric or gastro-oesophageal junction adenocarcinoma (REGARD): An international, randomised, multicentre, placebo-controlled, phase 3 trial.** *Lancet* 2014;383(9911):31-9.

Janjigian YY et al. **Nivolumab ± ipilimumab in pts with advanced (adv)/metastatic chemotherapy-refractory (CTx-R) gastric (G), esophageal (E), or gastroesophageal junction (GEJ) cancer: CheckMate 032 study.** *Proc ASCO* 2017;Abstract 4014.

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.

Pavlakakis 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.

Shah MA et al. **Andecaliximab/GS-5745 alone and combined with mFOLFOX6 in advanced gastric and gastroesophageal junction adenocarcinoma: Results from a phase 1 study.** *Clin Cancer Res* 2018;[Epub ahead of print].

Shah MA et al. **Results of a phase I study of GS-5745 in combination with mFOLFOX in patients with advanced unresectable gastric/GE junction tumors.** *Proc ASCO* 2016;Abstract 4033.

Wainberg ZA et al. **KEYNOTE-059 update: Efficacy and safety of pembrolizumab alone or in combination with chemotherapy in patients with advanced gastric or gastroesophageal (G/GEJ) cancer.** *Proc ESMO* 2017;Abstract LBA28_PR.

Wilke H et al. **Ramucirumab plus paclitaxel versus placebo plus paclitaxel in patients with previously treated advanced gastric or gastro-oesophageal junction adenocarcinoma (RAINBOW): A double-blind, randomised phase 3 trial.** *Lancet Oncol* 2014;15(11):1224-35.

Module 2: Pancreatic Adenocarcinoma

Bekaii-Saab T et al. **A phase Ib/II study of cancer stemness inhibitor napabucasin in combination with gemcitabine (gem) & nab-paclitaxel (nabPTX) in metastatic pancreatic adenocarcinoma (mPDAC) patients (pts).** *Proc ESMO World Congress GI* 2017;Abstract LBA-002.

Bekaii-Saab T et al. **CanStem111P trial: A phase III study of napabucasin (BBI-608) plus nab-paclitaxel (nab-PTX) with gemcitabine (gem) in adult patients with metastatic pancreatic adenocarcinoma (mPDAC).** *Proc ASCO* 2017;Abstract TPS4148.

Chen LT et al. **Final results of NAPOLI-1: A phase 3 study of nal-IRI (MM-398) ± 5-fluorouracil and leucovorin (5-FU/LV) vs 5-FU/LV in metastatic pancreatic cancer (mPAC) previously treated with gemcitabine-based therapy.** *Proc ESMO* 2016;Abstract 622PD.

Conroy T et al. **Unicancer GI PRODIGE 24/CCTG PA.6 trial: A multicenter international randomized phase III trial of adjuvant mFOLFIRINOX versus gemcitabine (gem) in patients with resected pancreatic ductal adenocarcinomas.** ASCO 2018;Abstract LBA4001.

Hammel P et al. **Phase II LAPACT trial of nab-paclitaxel (nab-P) plus gemcitabine (G) for patients with locally advanced pancreatic cancer (LAPC).** Gastrointestinal Cancers Symposium 2018;Abstract 204.

Sonbol MB et al. **Second-line treatment in patients with pancreatic ductal adenocarcinoma: A meta-analysis.** *Cancer* 2017;123(23):4680-6.

Van Tienhoven G et al. **Preoperative chemoradiotherapy versus immediate surgery for resectable and borderline resectable pancreatic cancer (PREOPANC-1): A randomized, controlled, multicenter phase III trial.** ASCO 2018;Abstract LBA4002.

Select Publications

Wang-Gillam A et al. **Characteristics of long-term survivors in a randomized phase III trial (NAPOLI-1) of patients with metastatic pancreatic ductal adenocarcinoma (mPDAC) treated with liposomal irinotecan (nal-IRI; MM-398) + 5-FU/LV.** Gastrointestinal Cancers Symposium 2017;Abstract 293.

Wang-Gillam A et al. **Nanoliposomal irinotecan with fluorouracil and folinic acid in metastatic pancreatic cancer after previous gemcitabine-based therapy (NAPOLI-1): A global, randomised, open-label, phase 3 trial.** *Lancet* 2016;387(10018):545-57.

Module 3: Hepatocellular Carcinoma

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.

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 GI* 2017;Abstract O-009.

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.

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.

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. **KEYNOTE-224: Pembrolizumab in patients with advanced hepatocellular carcinoma previously treated with sorafenib.** Gastrointestinal Cancers Symposium 2018;Abstract 209.

Zhu AX et al. **Pembrolizumab (pembro) in patients with advanced hepatocellular carcinoma (HCC): KEYNOTE-224 update.** 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.** ASCO 2018;Abstract 4003.

Module 4: Colorectal Cancer

A phase III study of BBI-608 in combination with 5-fluorouracil, leucovorin, irinotecan (FOLFIRI) in adult patients with previously treated metastatic colorectal cancer (CRC). NCT02753127

Andre T et al. **Nivolumab + ipilimumab combination in patients with DNA mismatch repair-deficient/microsatellite instability-high (dMMR/MSI-H) metastatic colorectal cancer (mCRC): First report of the full cohort from CheckMate-142.** Gastrointestinal Cancers Symposium 2018;Abstract 553.

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

Bendell J et al. **Phase 1b/II study of cancer stemness inhibitor napabucasin in combination with FOLFIRI +/- bevacizumab (bev) in metastatic colorectal cancer (mCRC) patients (pts).** ESMO World Congress on Gastrointestinal Cancer 2017;Abstract LBA-003.

Select Publications

Diaz LA et al. **Keynote-177: Phase 3, open-label, randomized study of first-line pembrolizumab (Pembro) versus investigator-choice chemotherapy for mismatch repair-deficient (dMMR) or microsatellite instability-high (MSI-H) metastatic colorectal carcinoma (mCRC).** *Gastrointestinal Cancers Symposium 2018;Abstract TPS877.*

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

Diaz LA et al. **Phase 3, open-label, randomized study of first-line pembrolizumab (pembro) vs investigator-choice chemotherapy for mismatch repair-deficient (dMMR) or microsatellite instability-high (MSI-H) metastatic colorectal carcinoma (mCRC): KEYNOTE-177.** *Proc ASCO 2017;Abstract TPS3618.*

Huijberts S et al. **BEACON CRC: Safety lead-in (SLI) for the combination of binimetinib (BINI), encorafenib (ENCO), and cetuximab (CTX) in patients (pts) with BRAF-V600E metastatic colorectal cancer (mCRC).** *Proc ESMO 2017;Abstract 517P.*

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.*

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.*

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.*

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.*

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):350-58.*