Addressing Current Questions and Controversies 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 proceedings from a CME symposium during the 2019 ASCO Annual Meeting explore the most significant therapeutic advances in the field of GI cancers by using the perspectives of leading experts on challenging cases and questions submitted by clinicians in the community to frame a relevant discussion of how this information has aided in the refinement of current routine clinical practice and ongoing research. This CME activity will help medical oncologists and other allied healthcare professionals find answers to the individualized questions and concerns that they frequently encounter and in turn provide high-quality cancer care.

LEARNING OBJECTIVES

- Develop a long-term care plan for individuals diagnosed with metastatic colorectal cancer, considering the patient's 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 gastroesophageal cancers.
- Consider age, performance status and other clinical and logistical factors in the selection of systemic therapy for patients with localized, locally advanced or metastatic pancreatic adenocarcinoma.
- Recall available clinical trial data with approved and investigational systemic interventions, and where appropriate, apply this information to the current clinical care of 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.
- Counsel appropriately selected patients with GI cancers about participation in ongoing clinical trials evaluating other novel therapeutic agents and strategies.

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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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MODERATOR — **Dr Love** is president and CEO of Research To Practice. Research To Practice receives funds in the form of educational grants to develop CME activities from the following commercial interests: AbbVie Inc, Acerta Pharma — A member of the AstraZeneca Group, Adaptive Biotechnologies, Agendia Inc, Agios Pharmaceuticals Inc, Amgen Inc, Ariad Pharmaceuticals Inc, Array BioPharma Inc, Astellas Pharma Global Development Inc, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Biodesix Inc, bioTheranostics Inc, Boehringer Ingelheim Pharmaceuticals Inc, Boston Biomedical Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, Daiichi Sankyo Inc, Dendreon Pharmaceuticals Inc, Eisai Inc, Exelixis Inc, Foundation Medicine, Genentech, Genmab, Genomic Health Inc, Gilead Sciences Inc, Guardant Health, Halozyme Inc, ImmunoGen Inc, Incyte Corporation, Infinity Pharmaceuticals Inc, Ipsen Biopharmaceuticals Inc, Janssen Biotech Inc, administered by Janssen Scientific Affairs LLC, Jazz Pharmaceuticals Inc, Kite Pharma Inc, Lexicon Pharmaceuticals Inc, Lilly, Loxo Oncology Inc, a wholly owned subsidiary of Eli Lilly & Company, Merck, Merrimack Pharmaceuticals Inc, Myriad Genetic Laboratories Inc, Natera Inc, Novartis, Oncopeptides, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Prometheus Laboratories Inc, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sandoz Inc, a Novartis Division, Sanofi Genzyme, Seattle Genetics, Sirtex Medical Ltd, Spectrum Pharmaceuticals Inc, Taiho Oncology Inc, Takeda Oncology, Tesaro, Teva Oncology, Tokai Pharmaceuticals Inc and Tolero Pharmaceuticals.

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This activity is supported by educational grants from Bayer HealthCare Pharmaceuticals, Boston Biomedical Inc and Tolero Pharmaceuticals, Celgene Corporation, Eisai Inc, Exelixis Inc, Genentech, Ipsen Biopharmaceuticals Inc, Lilly, Merck and Taiho Oncology Inc.

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: July 2019

Expiration date: July 2020

Select Publications

Module 1: Hepatocellular Carcinoma

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

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. **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. **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 R et al. **Results of KEYNOTE-240: Phase 3 study of pembrolizumab (Pembro) vs best supportive care (BSC) for second line therapy in advanced hepatocellular carcinoma (HCC).** *Proc ASCO* 2019;**Abstract 4004**.

Finn R et al. **IMbrave150: A randomized phase III study of 1L atezolizumab plus bevacizumab vs sorafenib in locally advanced or metastatic hepatocellular carcinoma.** *Proc ASCO* 2018;**Abstract TPS4141**.

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.

Kelley RK et al. **Alpha fetoprotein (AFP) response and efficacy outcomes in the phase III CELESTIAL trial of cabozantinib (C) versus placebo (P) in advanced hepatocellular carcinoma (HCC).** Gastrointestinal Cancers Symposium 2019;**Abstract 423**.

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

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.

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**.

Yau T et al. **Nivolumab (NIVO) + ipilimumab (IPI) combination therapy in patients (pts) with advanced hepatocellular carcinoma (aHCC): Results from CheckMate 040.** *Proc ASCO* 2019;**Abstract 4012**.

Zhu AX et al. **KEYNOTE-224: Pembrolizumab in patients with advanced hepatocellular carcinoma previously treated with sorafenib.** Gastrointestinal Cancers Symposium 2019;**Abstract 209**.

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**.

Module 2: Pancreatic Adenocarcinoma

Bekaii-Saab T et al. **Phase 1b/2 trial of cancer stemness inhibitor napabucasin (NAPA) + *nab*-paclitaxel (nPTX) and gemcitabine (gem) in metastatic pancreatic adenocarcinoma (mPDAC).** *Proc ASCO* 2018;**Abstract 4110**.

Bekaii-Saab T et al. **A phase 1b/II study of cancer stemness inhibitor napabucasin in combination with gemcitabine (gem) & *nab*-paclitaxel (*nab*ptx) in metastatic pancreatic adenocarcinoma (mpdac) patients (pts).** *Proc ESMO World Congress on Gastrointestinal Cancer* 2017;**Abstract LBA-002**.

Binder KAR et al. **A phase II, single arm study of maintenance rucaparib in patients with platinum-sensitive advanced pancreatic cancer and a pathogenic germline or somatic mutation in *BRCA1*, *BRCA2* or *PALB2*.** *Proc AACR* 2019;**Abstract CT234**.

Select Publications

Conroy T et al. **FOLFIRINOX or gemcitabine as adjuvant therapy for pancreatic cancer.** *N Engl J Med* 2018;379(25):2395-406.

Dean A et al. **A phase 1/2, open-label dose-escalation study of liposomal irinotecan (nal-IRI) plus 5-fluorouracil/leucovorin (5-FU/LV) and oxaliplatin (OX) in patients with previously untreated metastatic pancreatic cancer (mPAC).** *Proc ASCO* 2018;**Abstract 4111**.

Hingorani SR et al. **HALO 202: Randomized phase II study of PEGPH20 plus *nab*-paclitaxel/gemcitabine versus *nab*-paclitaxel/gemcitabine in patients with untreated, metastatic pancreatic ductal adenocarcinoma.** *J Clin Oncol* 2018;36(4):359-66.

Kindler HL et al. **Olaparib as maintenance treatment following first-line platinum-based chemotherapy (PBC) in patients (pts) with a germline BRCA mutation and metastatic pancreatic cancer (mPC): Phase III POLO trial.** *Proc ASCO* 2019;**Abstract LBA4**.

O'Hara MH et al. **A Phase Ib study of CD40 agonistic monoclonal antibody APX005M together with gemcitabine (Gem) and *nab*-paclitaxel (NP) with or without nivolumab (Nivo) in untreated metastatic ductal pancreatic adenocarcinoma (PDAC) patients.** *Proc AACR* 2019;**Abstract CT004**.

Ramanathan RK et al. **Phase IB/II randomized study of FOLFIRINOX plus pegylated recombinant human hyaluronidase versus FOLFIRINOX alone in patients with metastatic pancreatic adenocarcinoma: SWOG S1313.** *J Clin Oncol* 2019;37(13):1062-9.

Wang-Gillam A et al. **NAPOLI-1 phase 3 study of liposomal irinotecan in metastatic pancreatic cancer: Final overall survival analysis and characteristics of long-term survivors.** *Eur J Cancer* 2019;108;78-87.

Wang-Gillam A et al. **Dose modifications of liposomal irinotecan (nal-IRI) + 5-fluorouracil/leucovorin (5-FU/LV) in NAPOLI-1: Impact on efficacy.** Gastrointestinal Cancers Symposium 2018;**Abstract 388**.

Module 3: Gastric/Gastroesophageal Junction Cancers

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. **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.

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.

Kato K et al. **KEYNOTE-590: Phase III study of first-line chemotherapy with or without pembrolizumab for advanced esophageal cancer.** *Future Oncol* 2019;15(10):1057-66.

Klempner SJ et al. **Initial report of second-line FOLFIRI in combination with ramucirumab in advanced gastroesophageal adenocarcinomas: A multi-institutional retrospective analysis.** *Oncologist* 2019;24(4):475-82.

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**.

Lorenzen S et al. **FOLFIRI plus ramucirumab versus paclitaxel plus ramucirumab for patients with advanced or metastatic adenocarcinoma of the stomach or gastroesophageal junction as second-line therapy: Interim safety and efficacy results from the phase II RAMIRIS Study (AIO-STO-0415) of the German Gastric Group at AIO.** *Proc ASCO* 2019;**Abstract 4023**.

Muro K et al. **Efficacy and safety of ramucirumab (RAM) for metastatic gastric or gastroesophageal junction (GEJ) adenocarcinoma across age subgroups in two global phase 3 trials.** Gastrointestinal Cancers Symposium 2017;**Abstract 03**.

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.

Satoh T et al. **A phase 3 study of nivolumab (Nivo) in previously treated advanced gastric or gastric esophageal junction (G/GEJ) cancer (ATTRACTION-2): Two-years update data.** ***Proc ESMO*** 2018;**Abstract 617PD**.

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.

Select Publications

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**.

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 4: Colorectal Cancer

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**.

Bekaii-Saab T 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 World Congress on Gastrointestinal Cancer* 2018;**Abstract O-014**.

Bekaii-Saab T et al. **A phase 1b/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 on Gastrointestinal Cancer* 2017;**Abstract LBA-002**.

Bendell J et al. **Phase Ib/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**.

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**.

Gambardella V et al. **New molecular challenges in metastatic colorectal cancer.** *Medicographia* 2018;40(3):101-8.

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 (NIVO) + low-dose ipilimumab (IPI) in previously treated patients (pts) with microsatellite instability-high/mismatch repair-deficient (MSI-H/dMMR) metastatic colorectal cancer (mCRC): Long-term follow-up.** Gastrointestinal Cancers Symposium 2019;**Abstract 635**.

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.

Shitara K et al. **REVERCE: A randomized phase II study of regorafenib followed by cetuximab versus the reverse sequence for previously treated metastatic colorectal cancer patients.** *Ann Oncol* 2019;30(2):259-65.

Taieb J et al. **Safety and efficacy of trifluridine/tipiracil (FTD/TPI) in metastatic colorectal cancer (mCRC) patients according to previous treatment with regorafenib in the international phase 3b PRECONNECT study.** *Proc ESMO* 2018;**Abstract 464P**.

Van Cutsem E et al. **Binimetinib, encorafenib, and cetuximab triplet therapy for patients with BRAF V600E-mutant metastatic colorectal cancer: Safety lead-in results from the phase III BEACON colorectal cancer study.** *J Clin Oncol* 2019;37(17):1460-9.

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**.

Van Cutsem E et al; RECOURSE Study Group. **The subgroups of the phase III RECOURSE trial of trifluridine/tipiracil (TAS-102) versus placebo with best supportive care in patients with metastatic colorectal cancer.** *Eur J Cancer* 2018;90:63-72.

Venook A et al. **Impact of primary (1º) tumor location on overall survival (OS) and progression-free survival (PFS) in patients (pts) with metastatic colorectal cancer (mCRC): Analysis of CALGB/SWOG 80405 (Alliance).** *Proc ASCO* 2016;**Abstract 3504**.

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