# Cases from the Community

## Clinical Investigators Provide Their Perspectives on Emerging Research and Actual Patients with Gastrointestinal Cancers

## *A Special Video Supplement*

## CME Information

### TARGET AUDIENCE

This program is intended for medical oncologists, hematology-oncology fellows and other allied healthcare professionals involved in the treatment of colorectal, gastroesophageal, pancreatic and hepatocellular cancer.

### OVERVIEW OF ACTIVITY

Given the prevalent nature of the disease, extensive resources are allocated to colorectal cancer (CRC) research and education. Interestingly, however, although individually less frequently encountered, the collection of other "non-CRC" gastrointestinal (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.

This program features discussions with 2 faculty after a CME symposium held during the 2017 ASCO Annual Meeting regarding cases submitted by practicing general oncologists and review of the published literature surrounding the clinical situations explored. By providing information on the latest research developments and their potential impact on 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 for both CRC and select non-CRC GI cancers.

### LEARNING OBJECTIVES

- Develop a long-term care plan for individuals diagnosed with metastatic CRC, considering factors such as biomarker profile, exposure to prior systemic therapy, symptomatology and performance status.
- Evaluate recent data on therapeutic advances and changing practice standards in colorectal, gastric, pancreatic and hepatocellular cancer, and integrate this information, as appropriate, into current clinical care.
- Communicate the benefits and risks of existing and emerging systemic interventions to patients with locally advanced or metastatic hepatocellular cancer.
- Counsel patients regarding the management of side effects associated with commonly used systemic agents and regimens in the management of advanced colorectal, gastric, pancreatic and hepatocellular cancer.
- Recall the rationale for and clinical data with anti-PD-1 and/or anti-PD-L1 antibodies for patients with GI cancers.
- Describe the proposed mechanisms of action of and recall new data with investigational agents demonstrating promising activity in colorectal, gastric, pancreatic and hepatocellular cancer, and use this information to refer appropriate patients for participation in ongoing trials.

### ACCREDITATION STATEMENT

Research To Practice is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

### CREDIT DESIGNATION STATEMENT

Research To Practice designates this enduring material for a maximum of 2.5 *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

### 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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## HOW TO USE THIS CME ACTIVITY

This CME activity consists of a video component. To receive credit, the participant should watch the video, complete the Post-test with a score of 80% or better and fill out the Educational Assessment and Credit Form located at **ResearchToPractice.com/ASCOGastrointestinal17/Interviews/CME**.

## CONTENT VALIDATION AND DISCLOSURES

Research To Practice (RTP) is committed to providing its participants with high-quality, unbiased and state-of-the-art education. We assess conflicts of interest with faculty, planners and managers of CME activities. Conflicts of interest are identified and resolved through a conflict of interest resolution process. In addition, all activity content is reviewed by both a member of the RTP scientific staff and an external, independent physician reviewer for fair balance, scientific objectivity of studies referenced and patient care recommendations.

**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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**Consulting Agreements:** Bristol-Myers Squibb Company, MedImmune Inc, Roche Laboratories Inc, Sirtex Medical Ltd; **Contracted Research:** Amgen Inc, MedImmune Inc, Roche Laboratories Inc, Sirtex Medical Ltd; **Other Remunerated Activities:** Merck.

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**Contracted Research:** Amgen Inc, Bayer HealthCare Pharmaceuticals, Boehringer Ingelheim Pharmaceuticals Inc, Celgene Corporation, Ipsen Biopharmaceuticals Inc, Lilly, Merck, Novartis, Roche Laboratories Inc, Sanofi Genzyme.

**MODERATOR** — **Dr Love** is president and CEO of Research To Practice, which receives funds in the form of educational grants to develop CME activities from the following commercial interests: AbbVie Inc, Acerta Pharma, Adaptive Biotechnologies, Agendia Inc, Agios Pharmaceuticals Inc, Amgen Inc, Ariad Pharmaceuticals Inc, Array BioPharma Inc, Astellas Pharma Global Development Inc, AstraZeneca Pharmaceuticals LP, Baxalta Inc, Bayer HealthCare Pharmaceuticals, Biodesix Inc, bioTheranostics Inc, Boehringer Ingelheim Pharmaceuticals Inc, Boston Biomedical Pharma Inc, Bristol-Myers Squibb Company, Celgene Corporation, Clovis Oncology, CTI BioPharma Corp, Dendreon Pharmaceuticals Inc, Eisai Inc, Exelixis Inc, Foundation Medicine, Genentech BioOncology, Genomic Health Inc, Gilead Sciences Inc, 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, Medivation Inc, a Pfizer Company, Merck, Merrimack Pharmaceuticals Inc, Myriad Genetic Laboratories Inc, NanoString Technologies, Natera Inc, Novartis, Novocure, Onyx Pharmaceuticals, an Amgen subsidiary, Pfizer Inc, Pharmacyclics LLC, an AbbVie Company, Prometheus Laboratories Inc, Puma Biotechnology Inc, Regeneron Pharmaceuticals Inc, Sanofi Genzyme, Seattle Genetics, Sigma-Tau Pharmaceuticals Inc, Sirtex Medical Ltd, Spectrum Pharmaceuticals Inc, Taiho Oncology Inc, Takeda Oncology, Tesaro Inc, Teva Oncology and Tokai Pharmaceuticals Inc.

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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

**Last review date:** October 2017

**Expiration date:** October 2018

## Select Publications


Al-Batran SE et al. **Effect of neoadjuvant chemotherapy followed by surgical resection on survival in patients with limited metastatic gastric or gastroesophageal junction cancer: The AIO-FLOT3 Trial.** *JAMA Oncol* 2017;[Epub ahead of print].

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.** *Proc ASCO* 2016;**Abstract LBA4001**.

Andre T et al. **Combination of nivolumab (nivo) + ipilimumab (ipi) in the treatment of patients (pts) with deficient DNA mismatch repair (dMMR)/high microsatellite instability (MSI-H) metastatic colorectal cancer (mCRC): CheckMate 142 study.** *Proc ASCO* 2017;**Abstract 3531**.

**A phase III clinical trial of BBI608 plus weekly paclitaxel vs placebo plus weekly paclitaxel in adult patients with advanced, previously treated gastric and gastro-esophageal junction adenocarcinoma. NCT02178956**

Becerra C et al. **Phase Ib/II study of cancer stem cell (CSC) inhibitor BBI608 combined with paclitaxel in advanced gastric and gastroesophageal junction (GEJ) adenocarcinoma.** *Proc ASCO* 2015;**Abstract 4069**.

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.

Cainap C et al. **Linifanib versus sorafenib in patients with advanced hepatocellular carcinoma: Results of a randomized phase III trial.** *J Clin Oncol* 2015;33(2):172-9.

Cheng AL et al. **Sunitinib versus sorafenib in advanced hepatocellular cancer: Results of a randomized phase III trial.** *J Clin Oncol* 2013;31(32):4067-75.

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.

Crocenzi T et al. **Nivolumab (nivo) in sorafenib (sor)-naive and -experienced pts with advanced hepatocellular carcinoma (HCC): CheckMate 040 study.** *J Clin Oncol* 2017;35(15):4013.

Di Nicolantonio F et al. **Wild-type BRAF is required for response to panitumumab or cetuximab in metastatic colorectal cancer.** *J Clin Oncol* 2008;26(35):5705-12.

Dung L et al. **KEYNOTE-164: Phase 2 study of pembrolizumab for patients with previously treated, microsatellite instability-high advanced colorectal carcinoma.** *Proc ASCO* 2016;**Abstract TPS3631**.

El-Khoueiry A 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.

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**.

Grothey A et al. **Subgroup analysis of patients with metastatic colorectal cancer (mCRC) treated with regorafenib (REG) in the CORRECT trial who had progression-free survival (PFS) longer than 4 months.** *Proc ASCO* 2015;**Abstract 710**.

Grothey A et al. **Regorafenib monotherapy for previously treated metastatic colorectal cancer (CORRECT): An international, multicentre, randomised, placebo-controlled, phase 3 trial.** *Lancet* 2013;381(9863):303-12.

Grothey A et al. **Time course of regorafenib-associated adverse events in the phase III CORRECT study.** *Proc ASCO* 2013;**Abstract 467**.

Hingorani S et al. **Randomized phase II study of PEGPH20 plus *nab*-paclitaxel/gemcitabine (PAG) vs AG in patients (pts) with untreated, metastatic pancreatic ductal adenocarcinoma (mPDA).** *Proc ASCO* 2017;**Abstract 4008**.

Hingorani S et al. **Phase Ib study of PEGylated recombinant human hyaluronidase and gemcitabine in patients with advanced pancreatic cancer.** *Clin Cancer Res* 2016;22(12):2848-54.

Hong DS et al. **Phase Ib study of vemurafenib in combination with irinotecan and cetuximab in patients with metastatic colorectal cancer with BRAFV600E mutation.** *Cancer Discov* 2016;6(12):1352-65.

Ielpo B et al. **Preoperative treatment with gemcitabine plus *nab*-paclitaxel is a safe and effective chemotherapy for pancreatic adenocarcinoma.** *Eur J Surg Oncol* 2016;42(9):1394-400.

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**.

Jones JC et al. **Non-V600 BRAF mutations define a clinically distinct molecular subtype of metastatic colorectal cancer.** *J Clin Oncol* 2017;[Epub ahead of print].

## Select Publications


Le D et al. **Mismatch repair deficiency predicts response of solid tumors to PD-1 blockade.** *Science* 2017;357(6349):409-13.

Le DT et al. **PD-1 blockade in tumors with mismatch-repair deficiency.** *N Engl J Med* 2015;375(26):2509-20.

Li J et al. **Regorafenib plus best supportive care versus placebo plus best supportive care in Asian patients with previously treated metastatic colorectal cancer (CONCUR): A randomised, double-blind, placebo-controlled, phase 3 trial.** *Lancet Oncol* 2015;16(6):619-29.

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

Mayer R et al. **Randomized trial of TAS-102 for refractory metastatic colorectal cancer.** *N Engl J Med* 2015;372(20):1909-19.

Muro K et al. **Pembrolizumab for patients with PD-L1-positive advanced gastric cancer (KEYNOTE-012): A multicentre, open-label, phase 1b trial.** *Lancet Oncol* 2016;17(6):717-26.

Ohtsu A et al. **Onset of neutropenia as an indicator of treatment response in the phase III RECOURSE trial of TAS-102 vs placebo in patients with metastatic colorectal cancer.** *Proc ASCO* 2016;**Abstract 3556**.

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.

Punt CJ et al. **From tumour heterogeneity to advances in precision treatment of colorectal cancer.** *Nat Rev Clin Oncol* 2017;14(4):235-46.

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.

Suker M et al. **FOLFIRINOX for locally advanced pancreatic cancer: A systematic review and patient-level meta-analysis.** *Lancet Oncol* 2016;17(6):801-10.

Tejpar S et al. **Prognostic and predictive relevance of primary tumor location in patients with RAS wild-type metastatic colorectal cancer: Retrospective analyses of the CRYSTAL and FIRE-3 Trials.** *JAMA Oncol* 2016;[Epub ahead of print].

Vanwynsberghe H et al. **Predictive value of early tumor shrinkage and density reduction of lung metastases in patients with metastatic colorectal cancer treated with regorafenib.** *Clin Colorectal Cancer* 2017;[Epub ahead of print].

Vilgrain V et al. **SARAH: A randomised controlled trial comparing efficacy and safety of selective internal radiation therapy (with yttrium-90 microspheres) and sorafenib in patients with locally advanced hepatocellular carcinoma.** *J Hepatology* 2017;66(1):S85-6.

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.

Zhu A et al. **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.