Dissecting the Decision

Investigators Discuss the Available Data and Clinical Factors That Shape the Management of Gastrointestinal Cancers

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 (CRC) research and education. Interestingly, however, although individually less frequently encountered, the collection of other "non-CRC" GI cancers account for more per annum cancer-related deaths than those attributed to tumors of the colon and rectum combined. As such, educational opportunities relevant to the clinical management of both CRC and non-CRC GI tumors are essential to the general oncologist's delivery of comprehensive cancer care.

These video highlights from a CME symposium held during the 2017 Gastrointestinal Cancers Symposium feature presentations given by leading investigators in the management of GI cancers. By providing information on important new developments, this activity will address the most pressing educational needs of practitioners involved in the multidisciplinary management of colorectal, gastric, pancreatic and hepatocellular cancer.

LEARNING OBJECTIVES

- Appraise 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.
- Develop a long-term care plan for individuals with metastatic CRC considering biomarker profile, exposure to prior systemic therapy, symptomatology, performance status and personal goals for treatment.
- Use HER2 status, clinical factors and patient perspectives to optimize the selection and sequence of systemic therapy for patients with locally advanced or metastatic gastric or gastroesophageal cancer.
- Consider age, performance status and other clinical and logistical factors in the selection of systemic therapy for patients with locally advanced or metastatic pancreatic cancer.
- Communicate the benefits and risks of existing and emerging systemic interventions to patients with locally advanced or metastatic hepatocellular cancer.
- Communicate with patients and their caregivers regarding the incidence and manifestation of side effects and toxicities associated with commonly used systemic agents and regimens in the management of advanced colorectal, gastric, pancreatic and hepatocellular cancer.
- Appraise the rationale for and clinical data with investigational anti-PD-1 and 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 counsel appropriate patients regarding participation in ongoing clinical trials.

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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/GICancers17/CME**.

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Hardware/Software Requirements:
A high-speed Internet connection
A monitor set to 1280 x 1024 pixels or more
Internet Explorer 7 or later, Firefox 3.0 or later, Chrome, Safari 3.0 or later
Adobe Flash Player 10.2 plug-in or later
Adobe Acrobat Reader
(Optional) Sound card and speakers for audio

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Select Publications

PHILIP A PHILIP, MD, PHD

Barbour A et al. **Initial survival outcomes for the AGITG GAP study – a phase II study of perioperative *nab*-paclitaxel and gemcitabine for resectable pancreatic ductal adenocarcinoma (PDAC).** *Proc ASCO* 2016;**Abstract 4105**.

Blazer MA et al. **Tolerability and efficacy of modified FOLFIRINOX (mFOLFIRINOX) in patients with borderline-resectable pancreatic cancer (BRPC) and locally advanced unresectable pancreatic cancer (LAURPC).** *Proc ASCO* 2014;**Abstract 275**.

Carr RM, Fernandez-Zapico ME. **Pancreatic cancer microenvironment, to target or not to target?** *EMBO Mol Med* 2016;8(2):80-2.

Gill S et al. **PANCREOX: A randomized phase III study of 5-fluorouracil/leucovorin with or without oxaliplatin for second-line advanced pancreatic cancer in patients who have received gemcitabine-based chemotherapy.** *J Clin Oncol* 2016;34(32):3914-20.

Hackert T et al. **Locally advanced pancreatic cancer: Neoadjuvant therapy with Folfirinox results in resectability in 60% of the patients.** *Ann Surg* 2016;264(3):457-63.

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.

Kalra AV et al. **Preclinical activity of nanoliposomal irinotecan is governed by tumor deposition and intratumor prodrug conversion.** *Cancer Res* 2014;74(23):7003-13.

Katz MH et al. **Preoperative modified FOLFIRINOX treatment followed by capecitabine-based chemoradiation for borderline resectable pancreatic cancer: Alliance for Clinical Trials in Oncology trial A021101.** *JAMA Surg* 2016;151(8):e161137.

Ko AH. **Nanomedicine developments in the treatment of metastatic pancreatic cancer: Focus on nanoliposomal irinotecan.** *Int J Nanomedicine* 2016;11:1225-35.

Kushman M et al. **Full dose neoadjuvant FOLFIRINOX is associated with prolonged survival in patients with locally advanced pancreatic adenocarcinoma.** *Pancreatology* 2015;15(6):667-73.

Mahaseth H et al. **Modified FOLFIRINOX regimen with improved safety and maintained efficacy in pancreatic adenocarcinoma.** *Pancreas* 2013;42(8):1311-5.

Nanda RH et al. **Neoadjuvant modified FOLFIRINOX and chemoradiation therapy for locally advanced pancreatic cancer improves resectability.** *J Surg Oncol* 2015;111(8):1028-34.

Oettle H et al. **Second-line oxaliplatin, folinic acid, and fluorouracil versus folinic acid and fluorouracil alone for gemcitabine-refractory pancreatic cancer: Outcomes from the CONKO-003 trial.** *J Clin Oncol* 2014;32(23):2423-9.

Petrelli F et al. **FOLFIRINOX-based neoadjuvant therapy in borderline resectable or unresectable pancreatic cancer: A meta-analytical review of published studies.** *Pancreas* 2015;44(4):515-21.

Stein SM et al. **Final analysis of a phase II study of modified FOLFIRINOX in locally advanced and metastatic pancreatic cancer.** *Br J Cancer* 2016;114(7):737-43.

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.

Ueno M et al. **Phase II study of modified FOLFIRINOX for chemotherapy-naïve patients with metastatic pancreatic cancer.** *Proc ASCO* 2016;**Abstract 4111**.

Van Laethem J-L et al. **Preoperative gemcitabine-*nab*-paclitaxel (G-NP) for (borderline) resectable (BLR) or locally advanced (LA) pancreatic ductal adenocarcinoma (PDAC): Feasibility results and early response monitoring by diffusion-weighted (DW) MR.** *Proc ASCO* 2016;**Abstract 4116**.

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.

Wang-Gillam A et al. **Updated overall survival analysis of NAPOLI-1: Phase III study of nanoliposomal irinotecan (nal-IRI, MM-398), with or without 5-fluorouracil and leucovorin (5-FU/LV), versus 5-FU/LV in metastatic pancreatic cancer (mPAC) previously treated with gemcitabine-based therapy.** *Proc ASCO* 2016;**Abstract 417**.

Select Publications

TANIOS BEKAII-SAAB, MD

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**.

Cancer Genome Atlas Research Network. **Comprehensive molecular characterization of gastric adenocarcinoma.** *Nature* 2014;513(7517):202-9.

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.

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. **Bevacizumab in combination with chemotherapy as first-line therapy in advanced gastric cancer: A randomized, double-blind, placebo-controlled phase III study.** *J Clin Oncol* 2011;29(30):3968-76.

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.

Qin S et al. **Phase III study of apatinib in advanced gastric cancer: A randomized, double-blind, placebo-controlled trial.** *Proc ASCO* 2014;**Abstract 4003**.

Shah MA et al. **The BRIGHTER trial: A phase III randomized double-blind study of BBI-608 + weekly paclitaxel versus placebo (PBO) + weekly paclitaxel in patients (pts) with pretreated advanced gastric and gastro-esophageal junction (GEJ) adenocarcinoma.** *Proc ASCO* 2016;**Abstract TPS4144**.

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.

Yoon HH et al. **Ramucirumab combined with FOLFOX as front-line therapy for advanced esophageal, gastroesophageal junction, or gastric adenocarcinoma: A randomized, double-blind, multicenter Phase II trial.** *Ann Oncol* 2016;27(12):2196-203.

BERT H O'NEIL, MD

Bruix J et al. **Efficacy and safety of regorafenib versus placebo in patients with hepatocellular carcinoma (HCC) progressing on sorafenib: Results of the international, randomized phase 3 RESORCE trial.** *Ann Oncol* 2016;27(12):2196-203.

El-Khoueiry A et al. **Phase I/II safety and antitumor activity of nivolumab in patients with advanced hepatocellular carcinoma (HCC): CA209-040.** *Proc ASCO* 2015;**Abstract LBA101**.

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

Ray JB et al. **Regorafenib as a single-agent in the treatment of patients with gastrointestinal tumors: An overview for pharmacists.** *Target Oncol* 2015;10(2):199-213.

Wilhelm S et al. **BAY 43-9006 exhibits broad spectrum oral antitumor activity and targets the RAF/MEK/ERK pathway and receptor tyrosine kinases involved in tumor progression and angiogenesis.** *Cancer Res* 2004;64(19):7099-109.

JOHN L MARSHALL, MD

Bettington M et al. **The serrated pathway to colorectal carcinoma: Current concepts and challenges.** *Histopathology* 2013;62(3):367-86.

Guinney J et al. **The consensus molecular subtypes of colorectal cancer.** *Nat Med* 2015;21(11):1350-6.

Nordlinger B. **Perioperative FOLFOX4 chemotherapy and surgery versus surgery alone for resectable liver metastases from colorectal cancer (EORTC 40983): Long-term results of a randomised, controlled, phase 3 trial.** *Lancet Oncol* 2013;14(12):1208-15.

Primrose JN et al. **A randomized clinical trial of chemotherapy compared to chemotherapy in combination with cetuximab in k-RAS wild-type patients with operable metastases from colorectal cancer: The new EPOC study.** *Proc ASCO* 2013;**Abstract 3504**.

Venook AP 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**.

Select Publications

ERIC VAN CUTSEM, MD, PHD

Bendell JC et al. **Efficacy and tolerability in an open-label phase I/II study of MEK inhibitor trametinib (T), BRAF inhibitor dabrafenib (D), and anti-EGFR antibody panitumumab (P) in combination in patients (pts) with BRAF V600E mutated colorectal cancer (CRC).** *Proc ASCO* 2014;**Abstract 3515**.

Dienstmann R et al. **Consensus molecular subtypes and the evolution of precision medicine in colorectal cancer.** *Nat Rev Cancer* 2017;17(2):79-92.

Elez E et al. **Results of a phase 1b study of the selective BRAF V600 inhibitor encorafenib in combination with cetuximab alone or cetuximab + alpelisib for treatment of patients with advanced BRAF-mutant metastatic colorectal cancer.** *Proc WCGC* 2015;**Abstract LBA-08**.

Guinney J et al. **The consensus molecular subtypes of colorectal cancer.** *Nat Med* 2015;21(11):1350-6.

Hong DS et al. **Phase Ib study of vemurafenib in combination with irinotecan and cetuximab in patients with BRAF-mutated metastatic colorectal cancer and advanced cancers.** *Proc ASCO* 2015;**Abstract 3511**.

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**.

Punt C et al. **From tumour heterogeneity to advances in precision treatment of colorectal cancer.** *Nat Rev Clin Oncol* 2016;[Epub ahead of print].

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.

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JOHANNA C BENDELL, MD

Bendell JC et al. **Clinical activity and safety of cobimetinib (cobi) and atezolizumab in colorectal cancer (CRC).** *Proc ASCO* 2016;**Abstract 3502**.

Brahmer JR et al. **Phase I study of single-agent anti–programmed death-1 (MDX-1106) in refractory solid tumors: Safety, clinical activity, pharmacodynamics, and immunologic correlates.** *J Clin Oncol* 2010;28(19):3167-75.

Desai J et al. **Efficacy and safety of cobimetinib (cobi) and atezolizumab (atezo) in an expanded phase 1b study of microsatellite-stable (MSS) metastatic colorectal cancer (mCRC).** *Proc ESMO* 2016;**Abstract 470P**.

Ebert PJ et al. **MAP kinase inhibition promotes T cell and anti-tumor activity in combination with PD-L1 checkpoint blockade.** *Immunity* 2016;44(3):609-21.

Giannakis M et al. **Genomic correlates of immune-cell infiltrates in colorectal carcinoma.** *Cell Reports* 2016;7(4):1206.

Hamid O et al. **Anti-programmed death-1 and anti-programmed death-ligand 1 antibodies in cancer therapy.** *Exp Opin Biol Ther* 2013;13(6):847-61.

Hegde PS et al. **The where, the when, and the how of immune monitoring for cancer immunotherapies in the era of checkpoint inhibition.** *Clin Cancer Res* 2016;22(8):1865-74.

Jacobs J et al. **Immune checkpoint modulation in colorectal cancer: What's new and what to expect.** *J Immunol Res* 2015;2015:158038.

Keir ME et al. **PD-1 and its ligands in tolerance and immunity.** *Annu Rev Immunol* 2008;26:677-704.

Kim JM, Chen DS. **Immune escape to PD-L1/PD-1 blockade: Seven steps to success (or failure).** *Ann Oncol* 2016;27(8):1492-504.

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Select Publications

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Overman MJ et al. **Nivolumab ± ipilimumab in treatment (tx) of patients (pts) with metastatic colorectal cancer (mCRC) with and without high microsatellite instability (MSI-H): CheckMate-142 interim results.** *Proc ASCO* 2016;**Abstract 3501**.

Pardoll DM. **The blockade of immune checkpoints in cancer immunotherapy.** *Nat Rev Cancer* 2012;12(4):252-64.

Postow MA et al. **Nivolumab and ipilimumab versus ipilimumab in untreated melanoma.** *N Engl J Med* 2015;372(21):2006-17.

Topalian SL et al. **Safety, activity, and immune correlates of anti-PD-1 antibody in cancer.** *N Engl J Med* 2012;366(26):2443-54.

Wallin J et al. **Clinical activity and immune correlates from a phase Ib study evaluating atezolizumab (anti-PDL1) in combination with FOLFOX and bevacizumab (anti-VEGF) in metastatic colorectal carcinoma.** *Proc AACR* 2016;**Abstract 2651**.

Wang C et al. **In vitro characterization of the anti-PD-1 antibody nivolumab, BMS-936558, and in vivo toxicology in non-human primates.** *Cancer Immunol Res* 2014;2(9):846-56.

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