

REAL-LIFE DECISIONS

Clinical Investigators Provide Their Perspectives on Actual Patients with Metastatic Colorectal, Gastric and Pancreatic Cancer — A Special Roundtable Supplement

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

Local and systemic treatment approaches for GI cancers are continuously evolving. The impact of novel molecular-targeted and biologic therapies on the management of GI cancers has been profound and in several instances has changed best-practice care. In noncolorectal (non-CRC) GI cancers, late-stage clinical trials have demonstrated exciting results with an array of novel agents that are poised for integration into existing treatment algorithms. Also, a recent rapid expansion of novel biomarkers, multigene signatures and molecular-targeted systemic agents has significantly refined the clinical algorithm such that individualized therapeutic approaches have become standard for patients with colorectal cancer (CRC). This rapid paradigm shift presents a challenge to practicing oncologists who must grapple with the presentation of ambiguous data sets and their immediate impact on treatment decisions.

In addition to maintaining a sound understanding of the conventional but distinct treatment algorithms applicable to CRC and each subtype of non-CRC GI cancers, practicing oncologists must now rationally integrate targeted agents into their individualized therapeutic recommendations for the safe and effective clinical management of these diseases. By providing information on the latest research developments and their potential application to routine practice, this activity is designed to assist medical oncologists, surgeons and other healthcare providers with the formulation of up-to-date clinical management strategies for CRC and various non-CRC GI cancers.

LEARNING OBJECTIVES

- Develop a long-term treatment plan for individuals diagnosed with advanced CRC, considering the patient's biomarker profile, exposure to prior systemic therapy, symptomatology, performance status and treatment goals.

- Discuss the use of HER2 status and clinical factors to optimize the selection and sequence of systemic therapy for locally advanced or metastatic gastric/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.
- Recognize the recent FDA approvals of TAS-102 for metastatic CRC and nal-IRI (MM-398) for metastatic pancreatic cancer, and discuss strategies to safely incorporate these agents into current clinical algorithms.
- Review new data on investigational agents demonstrating promising activity in colorectal, gastric/gastroesophageal and pancreatic cancer.
- Discuss the role of immune checkpoint inhibitors in the management of GI cancers.

ACCREDITATION STATEMENT

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Successful completion of this CME activity enables the participant to earn up to 2.5 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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Consulting Agreements: Amgen Inc, Bayer HealthCare Pharmaceuticals, Boehringer Ingelheim Pharmaceuticals Inc, EMD Serono Inc, Genentech BioOncology, Lilly, Merrimack Pharmaceuticals Inc, Pfizer Inc, Taiho Oncology Inc; **Data and Safety Monitoring Board:** Exelixis Inc.

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Advisory Committee and Consulting Agreements: Bayer HealthCare Pharmaceuticals, EMD Serono Inc, Genentech BioOncology, Merck, Roche Laboratories Inc; **Contracted Research:** Bayer HealthCare Pharmaceuticals, Boehringer Ingelheim Pharmaceuticals Inc, EMD Serono Inc, Genentech BioOncology, Merck, Roche Laboratories Inc; **Other Remunerated Activities:** Takeda Oncology.

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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

- Bang YJ et al; ToGA Trial Investigators. **Trastuzumab in combination with chemotherapy versus chemotherapy alone for treatment of HER2-positive advanced gastric or gastro-oesophageal junction cancer (ToGA): A phase 3, open-label, randomised controlled trial.** *Lancet* 2010;376(9742):687-97.
- Barthélémy P et al. **Pertuzumab: Development beyond breast cancer.** *Anticancer Res* 2014;34(4):1483-91.
- Bekaii-Saab TS et al. **A phase Ib/II study of BBI608 combined with weekly paclitaxel in advanced pancreatic cancer.** Gastrointestinal Cancers Symposium 2016;Abstract 196.
- Bupathi M et al. **Irinotecan and infusional 5-fluorouracil (mFOLFIRI) in patients with refractory advanced pancreas cancer (APC): A single institution experience.** Gastrointestinal Cancers Symposium 2016;Abstract 215.
- Cancer Genome Atlas Research Network. **Comprehensive molecular characterization of gastric adenocarcinoma.** *Nature* 2014;513(7517):202-9.
- Chen L et al. **Expanded analyses of napoli-1: Phase 3 study of MM-398 (nal-IRI), with or without 5-fluorouracil and leucovorin, versus 5-fluorouracil and leucovorin, in metastatic pancreatic cancer (mPAC) previously treated with gemcitabine-based therapy.** Gastrointestinal Cancers Symposium 2015;Abstract 234.
- Conroy T et al. **FOLFIRINOX versus gemcitabine for metastatic pancreatic cancer.** *N Engl J Med* 2011;364(19):1817-25.
- Edenfeld W et al. **Molecular profiling of HER2-positive colorectal cancer for identification of multiple potential drug targets.** *Proc ASCO* 2014;Abstract e14508.
- Fuchs CS et al; REGARD Trial Investigators. **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.
- Gibbs P et al. **SIRFLOX: Randomized phase III trial comparing first-line mFOLFOX6 ± bevacizumab (bev) versus mFOLFOX6 + selective internal radiation therapy (SIRT) ± bev in patients (pts) with metastatic colorectal cancer (mCRC).** *Proc ASCO* 2015;Abstract 3502.
- Grothey A et al; CORRECT Study Group. **Regorafenib monotherapy for previously treated metastatic colorectal cancer (CORRECT): An international, multicentre, randomised, placebo-controlled, phase 3 trial.** *Lancet* 2013;381(9863):303-12.
- Gruenberger T et al. **Bevacizumab plus mFOLFOX-6 or FOLFOXIRI in patients with initially unresectable liver metastases from colorectal cancer: The OLIVIA multinational randomised phase II trial.** *Ann Oncol* 2015;26(4):702-8.
- Heinemann V et al. **Cetuximab-based or bevacizumab-based first-line treatment in patients with KRAS p.G13D mutated metastatic colorectal cancer (mCRC) — A meta-analysis of 54 cases.** *Proc ASCO* 2012;Abstract 511.
- Hingorani SR et al. **High response rate and PFS with PEGPH20 added to nab-paclitaxel/gemcitabine in stage IV previously untreated pancreatic cancer patients with high-HA tumors: Interim results of a randomized phase II study.** *Proc ASCO* 2015;Abstract 4006.
- Kemeny NE et al. **Conversion to resectability using hepatic artery infusion plus systemic chemotherapy for the treatment of unresectable liver metastases from colorectal carcinoma.** *J Clin Oncol* 2009;27(21):3465-71.
- Khoja L et al. **Evaluation of hypertension and proteinuria as markers of efficacy in antiangiogenic therapy for metastatic colorectal cancer.** *J Clin Gastroenterol* 2014;48(5):430-4.
- Ko AH et al. **A multinational phase 2 study of nanoliposomal irinotecan sucrosfate (PEP02, MM-398) for patients with gemcitabine-refractory metastatic pancreatic cancer.** *Br J Cancer* 2013;109(4):920-5.
- Loupakis F et al. **Initial therapy with FOLFOXIRI and bevacizumab for metastatic colorectal cancer.** *N Engl J Med* 2014;371(17):1609-18.
- Martin V et al. **HER2 gene copy number status may influence clinical efficacy to anti-EGFR monoclonal antibodies in metastatic colorectal cancer patients.** *Br J Cancer* 2013;108(3):668-75.
- Mayer RJ et al; RECURSE Study Group. **Randomized trial of TAS-102 for refractory metastatic colorectal cancer.** *N Engl J Med* 2015;372(20):1909-19.
- Mross K et al. **A phase I dose-escalation study of regorafenib (BAY 73-4506), an inhibitor of oncogenic, angiogenic, and stromal kinases, in patients with advanced solid tumors.** *Clin Cancer Res* 2012;18(9):2658-67.
- Muro K et al. **Relationship between PD-L1 expression and clinical outcomes in patients (Pts) with advanced gastric cancer treated with the anti-PD-1 monoclonal antibody pembrolizumab (Pembro; MK-3475) in KEYNOTE-012.** Gastrointestinal Cancers Symposium 2015;Abstract 03.

Select Publications

- Riccotta R et al. **Cavitation of lung metastases induced by regorafenib in patients with colorectal carcinoma: Data from the phase III CORRECT study.** *Proc ECCO 2015;Abstract 2015.*
- Saavedra E et al. **Dysphonia induced by anti-angiogenic compounds.** *Invest New Drugs 2014;32(4):774-82.*
- Shah M et al. **The BRIGHTER trial: A phase III randomized double-blind study of BBI608 + weekly paclitaxel versus placebo (PBO) + weekly paclitaxel in patients (pts) with pretreated advanced gastric and gastro-esophageal junction (GEJ) adenocarcinoma.** *Proc ASCO 2015;Abstract TPS4139.*
- Siena S et al. **Trastuzumab and lapatinib in HER2-amplified metastatic colorectal cancer patients (mCRC): The HERACLES trial.** *Proc ASCO 2015;Abstract 3508.*
- Sobrero AF et al. **EPIC: Phase III trial of cetuximab plus irinotecan after fluoropyrimidine and oxaliplatin failure in patients with metastatic colorectal cancer.** *J Clin Oncol 2008;26(14):2311-9.*
- Strumberg D, Schultheis B. **Regorafenib for cancer.** *Expert Opin Investig Drugs 2012;21(6):879-89.*
- Van Cutsem E et al. **HER2 screening data from ToGA: Targeting HER2 in gastric and gastroesophageal junction cancer.** *Gastric Cancer 2015;18(3):476-84.*
- Van Cutsem E et al. **Randomized phase III study of irinotecan and 5-FU/FA with or without cetuximab in the first-line treatment of patients with metastatic colorectal cancer (mCRC): The CRYSTAL trial.** *Proc ASCO 2007;Abstract 4000.*
- Von Hoff D et al. **NAPOLI-1: Randomized Phase 3 study of MM-398 (nal-IRI), with or without 5-fluorouracil and leucovorin, versus 5-fluorouracil and leucovorin, in metastatic pancreatic cancer progressed on or following gemcitabine-based therapy.** *ESMO World Congress on Gastrointestinal Cancer 2015;Abstract O-0003.*
- Von Hoff DD et al. **Increased survival in pancreatic cancer with nab-paclitaxel plus gemcitabine.** *N Engl J Med 2013;369(18):1691-703.*
- Weinberg BA et al. **Current standards and novel treatment options for metastatic pancreatic adenocarcinoma.** *Oncology (Williston Park) 2015;29(11):809-20, 886.*
- Wilhelm SM et al. **Regorafenib (BAY 73-4506): A new oral multikinase inhibitor of angiogenic, stromal and oncogenic receptor tyrosine kinases with potent preclinical antitumor activity.** *Int J Cancer 2011;129(1):245-55.*
- Wilke H et al; RAINBOW Study Group. **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.*
- Yaeger R et al. **Pilot trial of combined BRAF and EGFR inhibition in BRAF-mutant metastatic colorectal cancer patients.** *Clin Cancer Res 2015;21(6):1313-20.*