Cases from the Community

Clinical Investigators Provide Their Perspectives on Emerging Research and Actual Patients with 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 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.

These video proceedings from a CME symposium held during the 2017 ASCO Annual Meeting feature discussions with leading researchers regarding cases submitted on video 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

- 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 diagnosed with metastatic CRC, considering factors such as biomarker profile, exposure to prior systemic therapy, symptomatology, performance status and personal goals of 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.
- Counsel patients 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 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

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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 2.75 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

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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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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 Pharma-

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This activity is supported by educational grants from Astellas Pharma Global Development Inc, Bayer HealthCare Pharmaceuticals, Boston Biomedical Pharma Inc, Bristol-Myers Squibb Company, Celgene Corporation, Halozyme Inc, Ipsen Biopharmaceuticals Inc, Lilly and Taiho Oncology Inc.

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

Last review date: August 2017

Expiration date: August 2018

Select Publications

Axel Grothey, MD

Artale S et al. **Mutations of *KRAS* and *BRAF* in primary and matched metastatic sites of colorectal cancer.** *J Clin Oncol* 2008;26(25):4217-9.

Bertotti A et al. **A molecularly annotated platform of patient-derived xenografts ("xenopatients") identifies HER2 as an effective therapeutic target in cetuximab-resistant colorectal cancer.** *Cancer Discovery* 2011;1(6):508-23.

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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.

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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].

Kuwada SK et al. **Effects of trastuzumab on epidermal growth factor receptor-dependent and -independent human colon cancer cells.** *Int J Cancer* 2004;109(2):291-301.

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.

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].

Yarden Y, Sliwkowski MX. **Untangling the ErbB signalling network.** *Nat Rev Mol Cell Biol* 2001;2(2):127-37.

Eric Van Cutsem, MD, PhD

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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**.

Heiman F et al. **Real world data in oncology: Third- and fourth-line treatments administered in metastatic colon-rectal cancer (MCRC).** *Value Health* 2014;17(7):A644.

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.

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

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

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].

Gabriela Chiorean, MD

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**.

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**.

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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.

Select Publications

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.

Neuzillet C et al. **FOLFIRI regimen in metastatic pancreatic adenocarcinoma resistant to gemcitabine and platinum-salts.** *World J Gastroenterol* 2012;18(33):4533-41.

Stromnes IM et al. **Stromal reengineering to treat pancreas cancer.** *Carcinogenesis* 2014;35(7):1451-60.

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.

Van Laethem JL 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**.

Waddell N et al. **Whole genomes redefine the mutational landscape of pancreatic cancer.** *Nature* 2015;518(7540):495-501.

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.

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Anthony El-Khoueiry, MD

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.

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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.

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.

Johnson PJ et al. **Brivanib versus sorafenib as first-line therapy in patients with unresectable, advanced hepatocellular carcinoma: Results from the randomized phase III BRISK-FL study.** *J Clin Oncol* 2013;31(28):3517-24.

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

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Charles S Fuchs, MD, MPH

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

Select Publications

A randomised phase III double-blind placebo-controlled study of regorafenib in refractory advanced gastro-oesophageal cancer (AGOC). NCT02773524

A randomized, multicenter, open-label, phase 3 study of nivolumab plus ipilimumab or nivolumab in combination with oxaliplatin plus fluoropyrimidine versus oxaliplatin plus fluoropyrimidine in subjects with previously untreated advanced or metastatic gastric or gastroesophageal junction cancer. NCT02872116

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**.

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**.

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Randomized, double-blind, phase 3 study evaluating TAS-102 plus best supportive care (BSC) versus placebo plus BSC in patients with metastatic gastric cancer refractory to standard treatments. NCT02500043

Michael J Overman, MD

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Matsushita A et al. **Cancer exome analysis reveals a T-cell-dependent mechanism of cancer immunoediting.** *Nature* 2012; 482(7385):400-4.