

INTERACTIVE TUMOR BOARD

Clinical Investigators Discuss Available Research Shaping the Current and Future Treatment of Colorectal, Gastric and Pancreatic Cancer

CME Information

TARGET AUDIENCE

This activity is intended for medical oncologists, hematology-oncology fellows, surgeons and other healthcare providers involved in the treatment of colorectal, gastric and pancreatic 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 account for more per annum deaths than those attributed to tumors of the colon and rectum combined. As such, educational opportunities relevant to the clinical management of CRC and the most prevalent non-CRC GI tumors, including gastric and pancreatic cancer, are essential to the general oncologist’s delivery of comprehensive care.

These video proceedings from a CME meeting held during the 2018 Gastrointestinal Cancers Symposium feature review of actual cases of colorectal, gastric and pancreatic cancer from the practice of the moderator and presentations given by leading investigators in the management of GI cancers. By providing information and practical perspectives on important new developments, this activity will address the most pressing educational needs of practitioners involved in the multidisciplinary management of colorectal, gastric and pancreatic cancer.

LEARNING OBJECTIVES

- Review recent data on therapeutic advances and changing practice standards in colorectal, gastric and pancreatic cancer, and integrate this information, as appropriate, into current clinical care.
- Develop a long-term care plan for individuals diagnosed with metastatic CRC, considering biomarker profile, tumor location, exposure to prior systemic therapy, symptomatology, performance status (PS) and personal goals of treatment.
- Use HER2 status, clinical factors and patient perspectives to optimize the selection and sequence of systemic therapy for locally advanced or metastatic gastric/gastroesophageal cancer.

- Consider age, PS and other clinical and logistical factors in the selection of systemic therapy for patients with localized, locally advanced or metastatic pancreatic adenocarcinoma.
- Appraise the rationale for and clinical data with commercially available and developmental immune checkpoint inhibitors in the treatment of GI cancers.
- Describe ongoing research to validate or identify additional biomarkers predictive of response to anti-PD-1/PD-L1 antibodies, and use this information to guide future trial design or routine clinical practice.
- Recall the design of ongoing clinical trials evaluating novel investigational agents in GI cancers, and counsel appropriately selected patients about availability and participation.

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Please note, this program has been specifically designed for the following ABIM specialty: **medical oncology**.

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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:

Tanios Bekaii-Saab, MD

Professor, Mayo Clinic College of Medicine and Science
Co-Leader, GI Cancer Program, Mayo Clinic Cancer Center
Senior Associate Consultant
Mayo Clinic, Arizona
Scottsdale, Arizona

Consulting Agreements: Amgen Inc, ARMO BioSciences, Bayer HealthCare Pharmaceuticals, Bristol-Myers Squibb Company, Celgene Corporation, Exelixis Inc, Genentech BioOncology, Ipsen Biopharmaceuticals Inc, Merck, Roche Laboratories Inc, SillaJen; **Contracted Research:** Bayer HealthCare Pharmaceuticals, Boehringer Ingelheim Pharmaceuticals Inc, Boston Biomedical Pharma Inc, Bristol-Myers Squibb Company, Celgene Corporation, Lilly.

Peter C Enzinger, MD

Director, Center for Esophageal and Gastric Cancer
Assistant Professor of Medicine, Harvard Medical School
Dana-Farber Cancer Institute
Boston, Massachusetts

Advisory Committee: Merck; **Consulting Agreements:** Astellas Pharma Global Development Inc, Five Prime Therapeutics Inc, Merck, Taiho Oncology Inc.

Heinz-Josef Lenz, MD

Professor of Medicine and Preventive Medicine
J Terrence Lanni Chair in Cancer Research
Co-Director, USC Center for Molecular Pathways and Drug Discovery
Keck School of Medicine, University of Southern California
Associate Director of Adult Oncology
Co-Director, Colorectal Center

Scientific Director, Cancer Genetics Unit
USC Norris Comprehensive Cancer Center
Los Angeles, California

Advisory Committee and Consulting Agreements: Bayer HealthCare Pharmaceuticals, Bristol-Myers Squibb Company, EMD Serono Inc, Genentech BioOncology, Roche Laboratories Inc; **Contracted Research:** Bayer HealthCare Pharmaceuticals, Bristol-Myers Squibb Company, EMD Serono Inc, Genentech BioOncology, Merck, Roche Laboratories Inc.

Eileen M O'Reilly, MD

Associate Director, Clinical Research
David M Rubenstein Center for Pancreatic Cancer Research
Attending Physician, Member
Memorial Sloan Kettering Cancer Center
Professor of Medicine
Weill Medical College of Cornell University
New York, New York

Consulting Agreements: Agios Pharmaceuticals Inc, Amgen Inc, Aptus Clinical, ASLAN Pharmaceuticals, Astellas Pharma Global Development Inc, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Boston Scientific Corporation, Bristol-Myers Squibb Company, CARsgen, CASI Pharmaceuticals Inc, Celgene Corporation, CytomX Therapeutics, Daiichi Sankyo Inc, Debiopharm Group, Delcath Systems Inc, Eisai Inc, Gilead Sciences Inc, Halozyme Inc, Incyte Corporation, Inovio Pharmaceuticals Inc, Ipsen Biopharmaceuticals Inc, Lilly, MabVax Therapeutics, MedImmune Inc, Merck, Onxeo, PCI Biotech, Roche Laboratories Inc, Sanofi Genzyme, Servier, Silenseed Ltd, SillaJen, Sirtex Medical Ltd, Yakult Honsha Co Ltd; **Contracted Research:** Agios Pharmaceuticals Inc, Array BioPharma Inc, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, CASI Pharmaceuticals Inc, Celgene Corporation, Exelixis Inc, Genentech BioOncology, Incyte Corporation, Lilly, MabVax Therapeutics, MedImmune Inc, Momenta Pharmaceuticals Inc, Novartis, OncoMed Pharmaceuticals Inc, Roche Laboratories Inc.

Michael J Overman, MD

Associate Professor
Department of Gastrointestinal Medical Oncology
Division of Cancer Medicine
The University of Texas MD Anderson Cancer Center
Houston, Texas

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.

MODERATOR

Johanna C Bendell, MD

Director, GI Oncology Research
Associate Director, Drug Development Unit
Sarah Cannon Research Institute
Nashville, Tennessee

Contracted Research: Abbott Laboratories, AbbVie Inc, Agios Pharmaceuticals Inc, Apexigen, ARMO BioSciences, Array BioPharma Inc, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Boehringer Ingelheim Pharmaceuticals Inc, Boston Biomedical Pharma Inc, Bristol-Myers Squibb Company, Celgene Corporation, Celldex Therapeutics, CytomX Therapeutics, Daiichi Sankyo Inc, Eisai Inc, EMD Serono Inc, Five Prime Therapeutics Inc, Forty Seven Inc, Genentech BioOncology, Gilead Sciences Inc, GlaxoSmithKline, Incyte Corporation, Kolltan Pharmaceuticals Inc, Leap Therapeutics Inc, Lilly, MacroGenics Inc, MedImmune Inc, Merck, Nektar, Novartis, OncoMed Pharmaceuticals Inc, Onyx Pharmaceuticals, an Amgen subsidiary, Roche Laboratories Inc, Sanofi Genzyme, Stemcentrx, SynDevRx Inc, Taiho Oncology Inc, 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 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

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Select Publications

Heinz-Josef Lenz, MD

Goldstein J et al. **Multicenter retrospective analysis of metastatic colorectal cancer (CRC) with high-level microsatellite instability (MSI-H).** *Ann Oncol* 2014;25(5):1032-8.

Innocenti F et al. **Somatic DNA mutations, MSI status, mutational load (ML): Association with overall survival (OS) in patients (pts) with metastatic colorectal cancer (mCRC) of CALGB/SWOG 80405 (Alliance).** *Proc ASCO* 2017;Abstract 3504.

Kopetz S et al. **Randomized trial of irinotecan and cetuximab with or without vemurafenib in BRAF-mutant metastatic colorectal cancer (SWOG S1406).** *Proc ASCO* 2017;Abstract 3505.

Lee C et al. **Pancreatic cancer stem cells.** *J Clin Oncol* 2008;26(17):2806-12.

Li C et al. **Identification of pancreatic cancer stem cells.** *Cancer Res* 2007;67(3):1030-7.

Li Y et al. **Suppression of cancer relapse and metastasis by inhibiting cancer stemness.** *Proc Natl Acad Sci USA* 2015;112(6):1839-44.

S1613, a randomized phase II study of trastuzumab and pertuzumab (TP) compared to cetuximab and irinotecan (CETIRI) in advanced/metastatic colorectal cancer (mCRC) with HER-2 amplification. NCT03365882

Siena S et al. **Trastuzumab and lapatinib in HER2-amplified metastatic colorectal cancer patients (mCRC): The HERACLES trial.** *Proc ASCO* 2015;Abstract 3508.

Venderbosch S et al. **Mismatch repair status and BRAF mutation status in metastatic colorectal cancer patients: A pooled analysis of the CAIRO, CAIRO2, COIN, and FOCUS studies.** *Clin Cancer Res* 2014;20(20):5322-30.

Michael J Overman, MD

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.

Chalmers ZR et al. **Analysis of 100,000 human cancer genomes reveals the landscape of tumor mutational burden.** *Genome Med* 2017;9(1):34.

Conley BA et al. **Prevalence of mismatch repair deficiency (dMMR) in the NCI Molecular Analysis for Therapy Choice (NCI-MATCH or EAY131) population.** *Proc AACR Molecular Targets* 2017;Abstract A053.

Giannakis M et al. **Genomic correlates of immune-cell infiltrates in colorectal carcinoma.** *Cell Rep* 2016;15(4):857-65.

Kloor M, von Knebel Doeberitz M. **The immune biology of microsatellite-unstable cancer.** *Trends Cancer* 2016;2(3):121-33.

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

Overman MJ et al. **Nivolumab in patients with metastatic DNA mismatch repair-deficient or microsatellite instability-high colorectal cancer (CheckMate 142): An open-label, multicentre, phase 2 study.** *Lancet Oncol* 2017;18(9):1182-91.

Tabernero J et al. **Phase I studies of the novel carcinoembryonic antigen CD3 T-cell bispecific (CEA CD3 TCB) antibody as a single agent and in combination with atezolizumab: Preliminary efficacy and safety in patients with metastatic colorectal cancer (mCRC).** *Proc ASCO* 2017;Abstract 3002.

Yarchoan M et al. **Tumor mutational burden and response rate to PD-1 inhibition.** *N Engl J Med* 2017;377(25):2500-1.

Eileen M O'Reilly, MD

Gill S et al. **PANCREOX: A randomized phase III study of 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.

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* 2017;36(4):359-66.

Jaacobetz MA et al. **Hyaluronan impairs vascular function and drug delivery in a mouse model of pancreatic cancer.** *Gut* 2013;62(1):112-20.

Kaufman B et al. **Olaparib monotherapy in patients with advanced cancer and a germline BRCA1/2 mutation.** *J Clin Oncol* 2015;33(3):244-50.

Lowery M et al. **Phase II trial of veliparib in patients with previously treated BRCA-mutated pancreas ductal adenocarcinoma.** *Eur J Cancer* 2018;89:19-26.

Select Publications

Lowery MA et al. **Real-time genomic profiling of pancreatic ductal adenocarcinoma: Potential actionability and correlation with clinical phenotype.** *Clinical Cancer Res* 2017;23(20):6094-100.

Mandelker D et al. **Mutation detection in patients with advanced cancer by universal sequencing of cancer-related genes in tumor and normal DNA vs guideline-based germline testing.** *JAMA* 2017;318(9):825-35.

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.

O'Reilly EM et al. **Phase 1 trial evaluating cisplatin, gemcitabine, and veliparib in 2 patient cohorts: Germline BRCA mutation carriers and wild-type BRCA pancreatic ductal adenocarcinoma.** *Cancer* 2018;[Epub ahead of print].

Provenzano PP et al. **Enzymatic targeting of the stroma ablates physical barriers to treatment of pancreatic ductal adenocarcinoma.** *Cancer Cell* 2012;21(3):418-29.

Sonbol MB et al. **Second-line treatment in patients with pancreatic ductal adenocarcinoma: A meta-analysis.** *Cancer* 2017;123(23):4680-6.

Wang-Gillam A et al; NAPOLI-1 Study Group. **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.

Peter C Enzinger, MD

Abrams TA et al. **Patterns of chemotherapy (CT) use in a US-wide cohort of patients (pts) with metastatic gastric cancer (MGC).** *Gastrointestinal Cancers Symposium* 2018;Abstract 112.

Al-Batran S 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.

Bando H et al. **A multicenter phase II study of TAS-102 monotherapy in patients with pre-treated advanced gastric cancer (EPOC1201).** *Eur J Cancer* 2016;62:46-53.

Pavlakakis 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.

Shah MA et al. **Results of a phase I study of GS-5745 in combination with mFOLFOX in patients with advanced unresectable gastric/GE junction tumors.** *Proc ASCO* 2016;Abstract 4033.

Yashiro M, Matsuoka Y. **Fibroblast growth factor receptor signaling as therapeutic targets in gastric cancer.** *World J Gastroenterol* 2016;22(8):2415-23.

Tanios Bekaii-Saab, MD

Boku N et al. **A phase 3 study of nivolumab (nivo) in previously treated advanced gastric or gastroesophageal junction (G/GEJ) cancer: Updated results and subset analysis by PD-L1 expression (ATTRACTION-02).** *Proc ESMO* 2017;Abstract 6170.

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

Dong M et al. **Expression and prognostic roles of PIK3CA, JAK2, PD-L1, and PD-L2 in Epstein-Barr virus-associated gastric carcinoma.** *Hum Pathol* 2016;53:25-34.

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.

Kim JW et al. **Prognostic implications of immunosuppressive protein expression in tumors as well as immune cell infiltration within the tumor microenvironment in gastric cancer.** *Gastric Cancer* 2016;19(1):42-52.

Melero I et al. **Clinical development of immunostimulatory monoclonal antibodies and opportunities for combination.** *Clin Cancer Res* 2013;19(5):997-1008.

Tamura T et al. **Programmed death-1 ligand-1 (PDL1) expression is associated with the prognosis of patients with stage II/III gastric cancer.** *Anticancer Res* 2015;35(10):5369-76.

Tran PN et al. **PD-1 and PD-L1 as emerging therapeutic targets in gastric cancer: Current evidence.** *Gastrointest Cancer* 2017;7:1-11.

Zhang M et al. **The clinicopathological and prognostic significance of PD-L1 expression in gastric cancer: A meta-analysis of 10 studies with 1,901 patients.** *Sci Rep* 2016;6:37933.