

# Cases from the Community

## *Clinical Investigators Provide Perspectives on Actual Patients with Metastatic Colorectal, Gastric and Pancreatic Cancer*

### CME INFORMATION

#### TARGET AUDIENCE

This activity is intended for medical oncologists, hematology-oncology fellows, gastrointestinal surgeons and other healthcare providers involved in the treatment of gastrointestinal (GI) cancers.

#### OVERVIEW OF ACTIVITY

Cancer of the colon and rectum is the fourth most frequently diagnosed cancer and the second most common cause of death among all neoplasms in the United States, accounting for approximately 9% of all cancer deaths. Although individually less frequently encountered, the collection of other noncolorectal GI cancers account for more per annum cancer-related deaths than those attributed to tumors of the colon and rectum combined. In 2014 in the United States alone it is estimated that these diseases culminated in 136,830 new cases and 50,310 deaths.

Current therapeutic management of colorectal cancer (CRC) is dependent on tumor stage at the time of initial diagnosis, status of surgical margins, patient performance status, age, prior treatment exposure and sites of metastasis for those with disease recurrence or de novo advanced cancer. Although these variables are helpful in guiding selection of treatment, the introduction of novel biomarkers, multigene signatures and molecular-targeted systemic agents has significantly refined the clinical algorithm such that individualized therapeutic approaches have become the standard. Similarly, local and systemic treatment approaches for each of the non-CRC GI cancers are continuously evolving. Like their more prevalent tumor counterparts, the impact of novel molecular-targeted and biologic therapies on the management of non-CRC GI cancers has been profound. By providing information on the latest research developments and their potential application to routine practice, this activity is designed to assist medical oncologists, hematology-oncology fellows, gastrointestinal surgeons 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

- Coordinate comprehensive biomarker analysis for patients diagnosed with advanced CRC, and use this information to guide evidence-based care.

- Communicate the benefits and risks of approved anti-VEGF, anti-EGFR and other targeted biologic therapies to patients with metastatic CRC, and develop an evidence-based algorithm to sequence available options based on disease- and patient-specific characteristics.
- Individualize local and systemic treatment for patients with metastatic CRC that is isolated to the liver.
- Appreciate the recent FDA-approved indications for ramucirumab in advanced gastric or gastroesophageal junction cancer, and discern how this agent can be optimally integrated into clinical practice for patients with HER2-negative and HER2-positive disease.
- Implement a clinical plan for the management of advanced HER2-positive gastric cancer, incorporating existing and emerging targeted treatments.
- Appraise the rationale for and clinical data with investigational anti-PD-1 and/or anti-PD-L1 antibodies in patients with gastric cancer.
- Consider age, performance status and other clinical factors in the selection of systemic therapy for patients with metastatic pancreatic adenocarcinoma.
- Describe the mechanism of action of and available research data with ruxolitinib in pancreatic cancer, and use this information to counsel appropriate patients regarding ongoing trials evaluating this novel approach.
- Recall new data with other investigational agents demonstrating promising activity in colorectal, gastric and pancreatic cancers.

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**FACULTY** — The following faculty (and their spouses/partners) reported real or apparent conflicts of interest, which have been resolved through a conflict of interest resolution process:

### Dirk Arnold, MD

Director  
Department, Medical Oncology  
Klinik fuer Tumorbiologie  
Freiburg, Germany

**Advisory Committee:** Amgen Inc, Bayer HealthCare Pharmaceuticals, EMD Serono Inc, Roche Laboratories Inc;

**Consulting Agreement:** Sanofi; **Contracted Research:** EMD Serono Inc, Roche Laboratories Inc; **Speakers Bureau:** Bayer HealthCare Pharmaceuticals, EMD Serono Inc, Roche Laboratories Inc.

### Tanios Bekaii-Saab, MD

Section Chief, Gastrointestinal Oncology  
Chair, OSUCCC Gastrointestinal Disease Research Group  
Professor of Medicine and Pharmacy  
The Ohio State University – James Cancer Hospital  
Columbus, Ohio

**Consulting Agreements:** Amgen Inc, Bayer HealthCare Pharmaceuticals, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Genentech BioOncology, Lilly, Pfizer Inc, Taiho Oncology Inc; **Contracted Research:** Oncolytics Biotech Inc; **Other Remunerated Activities:** Exelixis Inc, Polaris Group.

### Johanna C Bendell, MD

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

No real or apparent conflicts of interest to disclose.

### Axel Grothey, MD

Professor of Oncology  
Department of Medical Oncology  
Mayo Clinic  
Rochester, Minnesota

**Contracted Research:** Bayer HealthCare Pharmaceuticals, Eisai Inc, Genentech BioOncology, Lilly, Pfizer Inc, Sanofi.

### Howard S Hochster, MD

Associate Director (Clinical Research)  
Yale Cancer Center  
Professor of Medicine  
Yale School of Medicine  
New Haven, Connecticut

**Advisory Committee:** Bayer HealthCare Pharmaceuticals, Genentech BioOncology; **Consulting Agreements:** Bayer HealthCare Pharmaceuticals, Genentech BioOncology, Genomic Health Inc, Roche Laboratories Inc, Sanofi; **Speakers Bureau:** Genomic Health Inc.

### Philip A Philip, MD, PhD

Professor of Oncology and Medicine  
Director of GI and Neuroendocrine Tumors  
Vice President of Medical Affairs  
Karmanos Cancer Institute  
Wayne State University  
Detroit, Michigan

**Advisory Committee:** Amgen Inc, Bayer HealthCare Pharmaceuticals, Bristol-Myers Squibb Company, Genentech BioOncology, Novartis Pharmaceuticals Corporation, Onyx Pharmaceuticals, an Amgen subsidiary; **Consulting Agreements:** Amgen Inc, Bayer HealthCare Pharmaceuticals, Boehringer Ingelheim Pharmaceuticals Inc, Bristol-Myers Squibb Company, Genomic Health Inc, Lilly, Novartis Pharmaceuticals Corporation, Onyx Pharmaceuticals, an Amgen subsidiary, Roche Laboratories Inc, Sanofi; **Contracted Research:** Amgen Inc, Bayer HealthCare Pharmaceuticals, Bristol-Myers Squibb Company, Celgene Corporation, Genentech BioOncology, Lilly, Novartis Pharmaceuticals Corporation, Onyx Pharmaceuticals, an Amgen subsidiary, Roche Laboratories Inc, Sanofi; **Speakers Bureau:** Amgen Inc, Bayer HealthCare Pharmaceuticals, Celgene Corporation, Genentech BioOncology, Novartis Pharmaceuticals Corporation, Onyx Pharmaceuticals, an Amgen subsidiary, Roche Laboratories Inc, Sanofi.

**CONSULTING MEDICAL ONCOLOGISTS** — The following consulting medical oncologists (and their spouses/partners) reported real or apparent conflicts of interest, which have been resolved through a conflict of interest resolution process:

### Lowell L Hart, MD

Scientific Director of Clinical Research  
Director, Drug Development Program  
Florida Cancer Specialists  
Fort Myers, Florida

**Contracted Research:** Genentech BioOncology, Lilly, Novartis Pharmaceuticals Corporation; **Speakers Bureau:** Genentech BioOncology, Novartis Pharmaceuticals Corporation.

### Neil I Morganstein, MD

Chair of Leukemia/Lymphoma Board  
Carol G Simon Cancer Center  
Overlook Medical Center  
Summit, New Jersey

No real or apparent conflicts of interest to disclose.

**Erik J Rupard, MD**

Chief, Section of Hematology-Oncology  
McGlenn Cancer Institute  
The Reading Hospital and Medical Center  
Reading, Pennsylvania

No real or apparent conflicts of interest to disclose.

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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

### Dirk Arnold, MD

**A two arm safety study of regorafenib before or after SIR-Spheres microspheres (90Y) for the treatment of patients with refractory metastatic colorectal cancer with liver metastases. [NCT02195011](#)**

**EPOCH: A phase III clinical trial evaluating TheraSphere® in patients with metastatic colorectal carcinoma of the liver who have failed first line chemotherapy. [NCT01483027](#)**

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**SIR-step: A randomised phase III trial comparing hepatic arterial injection of yttrium-90 resin microspheres (SIR-Spheres) plus systemic maintenance therapy versus systemic maintenance therapy alone for patients with unresectable liver metastases from colorectal cancer which are controlled after induction systemic therapy. [NCT01895257](#)**

### Tanios Bekaii-Saab, MD

**A randomized, multicenter, adaptive phase II/III study to evaluate the efficacy and safety of trastuzumab emtansine (T-DM1) versus taxane (docetaxel or paclitaxel) in patients with previously treated locally advanced or metastatic HER2-positive gastric cancer, including adenocarcinoma of the gastroesophageal junction. [NCT01641939](#)**

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Kang YK et al. **A phase IIa dose-finding and safety study of first-line pertuzumab in combination with trastuzumab, capecitabine and cisplatin in patients with HER2-positive advanced gastric cancer.** *Br J Cancer* 2014;111(4):660-6.

Lordick F et al. **Optimal chemotherapy for advanced gastric cancer: Is there a global consensus?** *Gastric Cancer* 2014;17(2):213-25.

Muro K et al. **Relationship between PD-L1 expression and clinical outcomes in patients with advanced gastric cancer treated with the anti-PD-1 monoclonal antibody pembrolizumab (Pembro; MK-3475) in KEYNOTE-012.** Gastrointestinal Cancers Symposium 2015;[Abstract 3](#).

Muro K et al. **A phase 1b study of pembrolizumab (Pembro; MK-3475) in patients with advanced gastric cancer.** *Proc ESMO* 2014;[Abstract LBA15](#).

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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.

#### **Johanna C Bendell, MD**

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Hurwitz H et al. **Results from a phase 2 study of ruxolitinib or placebo with capecitabine as second-line therapy in patients with metastatic pancreatic cancer: The RECAP trial.** ESMO 16<sup>th</sup> World Congress on Gastrointestinal Cancer 2014;[Abstract O-0026](#).

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.

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#### **Axel Grothey, MD**

**A randomized, open-label phase III Intergroup study: Effect of adding bevacizumab to cross over fluoropyrimidine based chemotherapy (CTx) in patients with metastatic colorectal cancer and disease progression under first-line standard CTx/bevacizumab combination.** [NCT00700102](#)

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#### **Howard S Hochster, MD**

**CONCUR:** A randomized, double-blind, placebo-controlled Phase III study of regorafenib plus best supportive care (BSC) versus placebo plus BSC in Asian subjects with metastatic colorectal cancer (CRC) who have progressed after standard therapy. [NCT01584830](#)

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**RECOURSE:** Randomized, double-blind, phase 3 study of TAS-102 plus best supportive care (BSC) versus placebo plus BSC in patients with metastatic colorectal cancer refractory to standard chemotherapies. [NCT01607957](#)

#### **Philip A Philip, MD, PhD**

A randomised open-label phase II study to assess the efficacy and safety of AZD4547 monotherapy versus paclitaxel in patients with advanced gastric adenocarcinoma (including adenocarcinoma of the lower third of the oesophagus or the gastro-oesophageal junction) with FGFR2 polysomy or gene amplification. [NCT01457846](#)

A randomized, double-blinded, placebo controlled, multicentre phase III study to assess the efficacy and safety of olaparib (AZD2281) in combination with paclitaxel, compared to placebo in combination with paclitaxel, in Asian patients with advanced gastric cancer (including the gastro-oesophageal junction) who have progressed following first line therapy. [NCT01924533](#)

A randomized, multicenter, adaptive Phase II/III study to evaluate the efficacy and safety of trastuzumab emtansine (T-DM1) versus taxane (docetaxel or paclitaxel) in patients with previously treated locally advanced or metastatic Her2-positive gastric cancer, including adenocarcinoma of the gastroesophageal junction. [NCT01641939](#)

A randomized, open-label, Japan-Korea collaborative phase 3 study to compare the efficacy of nimotuzumab and irinotecan combination therapy versus irinotecan monotherapy as second line treatment in subjects with advanced or recurrent gastric and gastroesophageal junction cancer. [NCT01813253](#)

**AVAGAST:** A double-blind, randomised, multicenter, phase III study of bevacizumab in combination with capecitabine and cisplatin versus placebo in combination with capecitabine and cisplatin, as first-line therapy in patients with advanced gastric cancer. [NCT00548548](#)

**BRIGHTER:** A phase III clinical trial of BBI608 plus weekly paclitaxel versus placebo plus weekly paclitaxel in adult patients with advanced, previously treated gastric and gastro-esophageal junction cancer. [NCT02178956](#)

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**ONO-4538 phase III study a multicenter, double-blind, randomized study in patients with unresectable advanced or recurrent gastric cancer.** [NCT02267343](#)

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**RILOMET-1: A phase 3, multicenter, randomized, double-blind, placebo controlled study of rilotumumab (AMG102) with epirubicin, cisplatin, and capecitabine (ECX) as first-line therapy in advanced MET-positive gastric or gastroesophageal junction adenocarcinoma.** [NCT01697072](#)

Tabernero J et al. **Pertuzumab with trastuzumab and chemotherapy in patients with HER2-positive metastatic gastric or gastroesophageal junction (GEJ) cancer: An international phase III study (JACOB).** *Proc ASCO* 2013;[Abstract TPS4150](#).

Waddell T et al. **Epirubicin, oxaliplatin, and capecitabine with or without panitumumab for patients with previously untreated advanced oesophagogastric cancer (REAL3): A randomised, open-label phase 3 trial.** *Lancet Oncol* 2013;14(6):481-9.

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.