

CONSENSUS OR CONTROVERSY?

CLINICAL INVESTIGATORS PROVIDE THEIR PERSPECTIVES ON PRACTICAL ISSUES AND RESEARCH QUESTIONS IN THE MANAGEMENT OF COLORECTAL, GASTRIC AND PANCREATIC CANCER

CME INFORMATION

TARGET AUDIENCE

This activity is intended for medical oncologists, hematology-oncology fellows and other allied healthcare professionals involved in the treatment of colorectal, gastric and pancreatic cancer.

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 will culminate 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 and other allied healthcare professionals 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 for these patients.
- Communicate the benefits and risks of anti-VEGF, anti-EGFR and other targeted biologic therapies to patients with metastatic CRC, and develop an evidence-based algorithm to sequence available therapeutic options.
- Individualize local and systemic treatment for patients with metastatic CRC that is isolated to the liver.
- Effectively integrate the evidence-based use of chemotherapy and molecular-targeted agents into the individualized management of advanced pancreatic cancer.
- Use clinical and molecular biomarkers to select optimal treatment strategies for patients with locally advanced or metastatic gastric or gastroesophageal junction (GEJ) cancer.
- Appreciate the recent FDA-approved indication for ramucirumab in advanced gastric or GEJ cancer, and discern how this agent can be optimally integrated into clinical practice.
- Recall new data with 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:

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Advisory Committee: Celgene Corporation, Genentech BioOncology, Lilly, Metamark Genetics Inc, Sanofi, Takeda Pharmaceuticals North America Inc; **Consulting Agreements:** ImClone Systems, a wholly owned subsidiary of Eli Lilly and Company, Lilly.

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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

Charles S Fuchs, MD, MPH

A phase III randomized trial of FOLFOXIRI + bevacizumab versus FOLFIRI + bevacizumab as first-line treatment for metastatic colorectal cancer. NCT00719797

A phase III trial of irinotecan/5-FU/leucovorin or oxaliplatin/5-FU/leucovorin with bevacizumab, or cetuximab (C225), or with the combination of bevacizumab and cetuximab for patients with untreated metastatic adenocarcinoma of the colon or rectum. NCT00265850

Douillard J et al. **Final results from PRIME: Randomized phase III study of panitumumab (pmab) with FOLFOX4 for first-line metastatic colorectal cancer (mCRC).** *Proc ASCO 2011;Abstract 3510.*

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Multicenter randomized trial evaluating FOLFIRI plus cetuximab versus FOLFIRI plus bevacizumab in first line treatment of metastatic colorectal cancer. NCT00433927

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Eric Van Cutsem, MD, PhD

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A double-blind, placebo-controlled, randomized, multicenter Phase III study evaluating the efficacy and safety of pertuzumab in combination with trastuzumab and chemotherapy in patients with HER2-positive metastatic gastroesophageal junction or gastric cancer. NCT01774786

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- A phase 1, dose escalation study of MGAH22 in patients with refractory HER2 positive breast cancer and patients with other HER2 positive carcinomas for whom no standard therapy is available. NCT01148849
- A phase I study of LJM716 in patients with squamous cell carcinoma of head and neck, or HER2-overexpressing metastatic breast cancer or gastric cancer. NCT01598077
- A phase I-II study to assess the safety, efficacy and pharmacokinetic profile of HM781-36B combined with paclitaxel and trastuzumab in patients with HER-2 positive advanced gastric cancer. NCT01746771
- A phase II open label trial of PF-00299804 monotherapy in patients with HER-2 positive advanced gastric cancer after failure of at least one prior chemotherapy regimen. NCT01152853
- A phase II study of afatinib (BIBW 2992) and trastuzumab in patients with advanced HER2-positive trastuzumab-refractory advanced esophagogastric cancer. NCT01522768
- A phase II study of trastuzumab in combination with capecitabine and oxaliplatin (XELOX) in patients with advanced gastric cancer. NCT01396707
- A phase II study of trastuzumab in combination with TS-ONE and cisplatin in firstline human epidermal growth factor receptor 2 (HER2)-positive advanced gastric cancer. NCT01736410
- A phase III, randomized, double-blinded study of IMC-1121B and best supportive care (BSC) versus placebo and BSC in the treatment of metastatic gastric or gastroesophageal junction adenocarcinoma following disease progression on first-line platinum- or fluoropyrimidine-containing combination therapy. NCT00917384
- A phase III study for ErbB2-positive advanced or metastatic gastric, esophageal, or gastroesophageal junction adenocarcinoma treated with capecitabine plus oxaliplatin with or without lapatinib. NCT00680901
- A phase III trial evaluating the addition of trastuzumab to trimodality treatment of HER2-overexpressing esophageal adenocarcinoma.
- A randomized, multicenter, open-label, phase III study of lapatinib (GW572016) in combination with weekly paclitaxel versus weekly paclitaxel alone in the second-line treatment of ErbB2-amplified advanced gastric cancer. NCT00486954
- A study of trastuzumab in combination with TS-ONE and cisplatin in first-line human epidermal growth factor receptor 2 (HER2)-positive advanced gastric cancer. NCT01228045
- An open-label, multi-center study to evaluate the disease free survival rate of a perioperative combination of capecitabine (Xeloda), trastuzumab (Herceptin) and oxaliplatin (XELOX-trastuzumab) in patients with resectable gastric or gastro-esophageal junction adenocarcinoma. NCT01130337
- An open-label, randomized, multicenter phase IIA study evaluating pertuzumab in combination with trastuzumab and chemotherapy in patients with HER2-positive advanced gastric cancer. NCT01461057
- An open-label, single-arm, multi-center phase II study to evaluate the efficacy and safety of AU922 in combination with trastuzumab standard therapy as second-line treatment in patients with HER2-positive advanced gastric cancer. NCT01402401
- An open-label, single arm study to evaluate the efficacy and safety of trastuzumab in combination with capecitabine and oxaliplatin (XELOX) as a first-line chemotherapy for inoperable, locally advanced or recurrent and/or metastatic gastric cancer. NCT01364493
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Phase 1 study of IMC-1121B in patients with advanced solid tumors. NCT01005355

Phase I study of weekly anti-vascular endothelial growth factor receptor 2 (VEGFR-2) monoclonal antibody IMC-1121B in patients with advanced solid tumors who have not responded to standard therapy. NCT00793975

Phase I trial of afatinib in combination with 3 weekly trastuzumab in patients with tumours overexpressing HER2. Once the MTD of afatinib with 3 weekly trastuzumab was established the safety of this dose will be assessed also in combination with weekly trastuzumab. NCT01649271

Phase I trial of interleukin-12 in combination with paclitaxel plus Herceptin in patients with HER2-positive malignancies. NCT00028535

Phase I trial of intraperitoneal ²¹²Pb-TCMC-trastuzumab for HER-2 expressing malignancy. NCT01384253

Phase II open label study to evaluate the biological activity of ASLAN001 (ARRY 334543) in patients with recurrent/metastatic gastric, gastro-oesophageal junction, and oesophageal carcinoma whose tumours are epidermal growth factor receptor-2 (HER-2) amplified or co-expressing epidermal growth factor receptor-1 (HER-1) and HER-2. NCT01614522

Phase II study of docetaxel, oxaliplatin, capecitabine with bevacizumab and trastuzumab in case of human epidermal growth factor receptor 2 (HER2)-positivity in patients with locally advanced or metastatic gastric cancer or adenocarcinoma of the gastro-oesophageal junction (B-DOCT study). NCT01359397

Phase II study to assess the efficacy and safety of trastuzumab in combination with XELOX as first-line treatment of patients with advanced or metastatic gastric cancer or gastro-esophageal junction, (HER2)-positive. NCT01503983

Phase II trial of CAPOX, bevacizumab and trastuzumab for patients with HER2-positive metastatic esophagogastric cancer. NCT01191697

Randomized, open label, phase 2 study of MM-111 and paclitaxel with trastuzumab in patients with HER2 positive carcinomas of the distal esophagus, gastroesophageal (GE) junction and stomach who have failed front line metastatic or locally advanced therapy. NCT01774851

Randomized, placebo-controlled, double-blind phase 2 study of mFOLFOX6 chemotherapy plus ramucirumab drug product (IMC-1121B) versus mFOLFOX6 plus placebo for advanced adenocarcinoma of the esophagus, gastroesophageal junction or stomach. NCT01246960

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