

Novel and Emerging Strategies in the Management of Gastrointestinal Cancers

CME Information

TARGET AUDIENCE

This activity is intended for medical oncologists and other healthcare providers involved in the treatment of gastrointestinal (GI) cancers.

OVERVIEW OF ACTIVITY

The pace of oncology drug development has accelerated in recent years to previously unmatched levels. Fueled by an increased understanding of the biologic underpinnings of tumor development and progression, clinical research platforms largely focused on evaluating the potential benefits of novel targeted therapeutics possessing unique mechanisms of action and safety profiles have led to improved outcomes in a myriad of large and rigorous clinical trials. Although this dynamic appears to be prevalent in many corners of oncology, recent advancements in the management of several prominent GI cancers have made it particularly pronounced in this area.

The successes yielded by this rational approach to the design and evaluation of new therapies have provided medical oncologists and patients with many beneficial treatments, but the availability of this growing list of novel options may also pose a challenge to the practicing clinician who must maintain knowledge of appropriate clinical management strategies across a vast spectrum of liquid and solid tumors. To bridge the gap between research and patient care, this video presentation by Philip A Philip uses a review of recent relevant publications and presentations, ongoing clinical trials and clinical investigator treatment preferences to assist medical oncologists and other healthcare providers involved in the treatment of GI cancers with the formulation of up-to-date clinical management strategies.

LEARNING OBJECTIVES

- Appraise the biologic rationale for and available clinical data with approved and investigational anti-PD-1 and/or anti-PD-L1 antibodies in the treatment of select GI cancers.
- Appreciate the rationale for and clinical evidence supporting the integration of novel treatment approaches for early pancreatic cancer.
- Recognize the mechanism of action of and available data with nanoliposomal irinotecan in the management of treatment-refractory metastatic pancreatic cancer, and develop strategies to incorporate this agent into patient-care algorithms.
- Consider available clinical research data documenting the efficacy of ramucirumab in metastatic colorectal and gastric or gastroesophageal junction cancers, and discern how this agent can be optimally integrated into clinical practice for patients with these diseases.
- Formulate a plan to include information about the left or right sidedness of colon cancer tumors in prognostication and systemic treatment decision-making.
- Develop an understanding of emerging Phase III efficacy data with commercially available multikinase inhibitors (eg, regorafenib and lenvatinib) for the management of relapsed/refractory hepatocellular carcinoma.
- Evaluate available Phase III data with peptide receptor radionuclide therapy with ¹⁷⁷Lu-Dotatate for patients with GI neuroendocrine tumors progressing on somatostatin analogue therapy.
- Appreciate the FDA-approved indication for telotristat ethyl, and consider this information in the selection of patients with carcinoid syndrome-associated diarrhea who might benefit from treatment with this agent.
- Recall available and emerging data with other investigational agents currently in Phase III testing for various GI cancers, and, where applicable, refer eligible patients for trial participation or expanded access programs.

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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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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

- 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.
- Bekaii-Saab T et al. **Identifying and targeting cancer stem cells in the treatment of gastric cancer.** *Cancer* 2017;123(8):1303-12.
- Bennouna J et al; ML18147 Study Investigators. **Continuation of bevacizumab after first progression in metastatic colorectal cancer (ML18147): A randomised phase 3 trial.** *Lancet Oncol* 2013;14(1):29-37.
- Bruix J et al; RESORCE Investigators. **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.
- Chen LT 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.*
- Diaz LA Jr et al. **KEYNOTE-177: Randomized phase III study of pembrolizumab versus investigator-choice chemotherapy for mismatch repair-deficient or microsatellite instability-high metastatic colorectal carcinoma.** *Gastrointestinal Cancers Symposium 2017;Abstract TPS815.*
- Dung TL et al. **Programmed death-1 blockade in mismatch repair deficient colorectal cancer.** *Proc ASCO* 2016;Abstract 103.
- 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.
- Finn RS et al. **KEYNOTE-240: Randomized phase III study of pembrolizumab versus best supportive care for second-line advanced hepatocellular carcinoma.** *Gastrointestinal Cancers Symposium 2017;Abstract TPS503.*
- Giannakis M et al. **Genomic correlates of immune-cell infiltrates in colorectal carcinoma.** *Cell Reports* 2016;15(4):857-65.
- Hackert T et al. **Locally advanced pancreatic cancer: Neoadjuvant therapy with folfinirox results in resectability in 60% of the patients.** *Ann Surg* 2016;264(3):457-63.
- Hegde PS et al. **The where, the when, and the how of immune monitoring for cancer immunotherapies in the era of checkpoint inhibition.** *Clin Cancer Res* 2016;22(8):1865-74.
- Imai K, Yamamoto H. **Carcinogenesis and microsatellite instability: The interrelationship between genetics and epigenetics.** *Carcinogenesis* 2008;29(4):673-80.
- Kang YK et al. **Nivolumab (ONO-4538/BMS-936558) as salvage treatment after second or later-line chemotherapy for advanced gastric or gastro-esophageal junction cancer (AGC): A double-blinded, randomized, phase III trial.** *Gastrointestinal Cancers Symposium 2017;Abstract 2.*
- Katz MH et al. **Preoperative modified FOLFIRINOX treatment followed by capecitabine-based chemoradiation for borderline resectable pancreatic cancer: Alliance for Clinical Trials in Oncology trial A021101.** *JAMA Surg* 2016;151(8):e161137.
- Kim JM, Chen DS. **Immune escape to PD-L1/PD-1 blockade: Seven steps to success (or failure).** *Ann Oncol* 2016;27(8):1492-504.
- Kwekkeboom DJ, Krenning EP. **Peptide receptor radionuclide therapy in the treatment of neuroendocrine tumors.** *Hematol Oncol Clin N Am* 2016;30(1):179-91.
- Llosa NJ et al. **The vigorous immune microenvironment of microsatellite instable colon cancer is balanced by multiple counter-inhibitory checkpoints.** *Cancer Discov* 2015;5(1):43-51.
- Molina-Cerrillo J et al. **Inhibition of peripheral synthesis of serotonin as a new target in neuroendocrine tumors.** *Oncologist* 2016;21(6):701-7.
- Neoptolemos JP et al; European Study Group for Pancreatic Cancer. **Comparison of adjuvant gemcitabine and capecitabine with gemcitabine monotherapy in patients with resected pancreatic cancer (ESPAC-4): A multicentre, open-label, randomised, phase 3 trial.** *Lancet* 2017;389(10073):1011-24.
- Neoptolemos JP et al. **A randomized, double-blind trial evaluating the palliative benefit of either continuing pamidronate or switching to zoledronate in patients with high-risk bone metastases from breast cancer (The Odyssey Study).** *Proc ASCO* 2016;Abstract LBA4006.
- Overman MJ et al. **Nivolumab ± ipilimumab in treatment (tx) of patients (pts) with metastatic colorectal cancer (mCRC) with and without high microsatellite instability (MSI-H): CheckMate-142 interim results.** *Proc ASCO* 2016;Abstract 3501.

Petrelli F et al; Gruppo Italiano per lo Studio dei Carcinomi dell'Apparato Digerente (GISCAD). **FOLFIRINOX-based neoadjuvant therapy in borderline resectable or unresectable pancreatic cancer: A meta-analytical review of published studies.** *Pancreas* 2015;44(4):515-21.

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.

Tabernero J et al; RAISE Study Investigators. **Ramucirumab versus placebo in combination with second-line FOLFIRI in patients with metastatic colorectal carcinoma that progressed during or after first-line therapy with bevacizumab, oxaliplatin, and a fluoropyrimidine (RAISE): A randomised, double-blind, multicentre, phase 3 study.** *Lancet Oncol* 2015;16(5):499-508.

Van Cutsem E et al. **Addition of aflibercept to fluorouracil, leucovorin, and irinotecan improves survival in a phase III randomized trial in patients with metastatic colorectal cancer previously treated with an oxaliplatin-based regimen.** *J Clin Oncol* 2012;30(28):3499-506.

Venook A et al. **Effect of first-line chemotherapy combined with cetuximab or bevacizumab on overall survival in patients with KRAS wild-type advanced or metastatic colorectal cancer: A randomized clinical trial.** *JAMA* 2017;317(23):2393-401.

Venook A et al. **Primary tumor location as an independent prognostic marker from molecular features for overall survival in patients with metastatic colorectal cancer: Analysis of CALGB/SWOG 80405 (Alliance).** *Proc ASCO* 2017;Abstract 3503.

Venook A et al. **Impact of primary (1°) tumor location on overall survival (OS) and progression-free survival (PFS) in patients (pts) with metastatic colorectal cancer (mCRC): Analysis of CALGB/SWOG 80405 (Alliance).** *Proc ASCO* 2016;Abstract 3504.

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.