Cases from the Community

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

A special audio supplement to a CME conference held during the 2015 Gastrointestinal Cancers Symposium featuring expert comments on the application of emerging research to patient care

Faculty Interviews

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From the publishers of:

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Cases from the Community: *Clinical Investigators Provide Perspectives on Actual Patients with Metastatic Colorectal, Gastric and Pancreatic Cancer*

A Continuing Medical Education Activity

OVERVIEW OF ACTIVITY

Colorectal cancer (CRC) is a common and potentially lethal type of cancer, and its clinical management is continuously evolving. Although "non-CRC" gastrointestinal (GI) and pancreatic tumors are less frequently encountered individually, the cancer-related deaths in these subcategories surpass those attributed to CRC. Recently published randomized, controlled studies have led to the emergence of novel biomarkers and new therapeutic targets and regimens, thereby altering existing management algorithms. A number of pivotal data sets illustrating the benefits of several novel agents indicate that additional therapeutic options may soon be available that will warrant consideration. In order to offer optimal patient care — including the option of clinical trial participation — the practicing medical oncologist must be well informed of these advances. This CME program uses one-on-one interviews with 2 leading GI clinical investigators who served as faculty at a recent satellite symposium to discuss cases and questions submitted by attendees. This program will assist practicing clinicians in formulating up-to-date and appropriate clinical management strategies.

LEARNING OBJECTIVES

- Effectively apply the results of practice-changing clinical research to the selection and sequencing of chemobiologic regimens for patients with metastatic CRC.
- Educate patients with metastatic gastric or pancreatic cancer regarding approved and novel treatment approaches and their associated risks and benefits.
- Appreciate the recent FDA-approved indications for ramucirumab alone or in combination with paclitaxel for advanced gastric or gastroesophageal junction cancer, and discern how this agent can be optimally integrated into clinical practice.
- Implement a clinical plan for the management of advanced HER2-positive gastric cancer, incorporating existing and emerging treatments.
- Recall new data with investigational agents demonstrating promising activity in colorectal, gastric and pancreatic cancers.

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CME INFORMATION

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SELECT PUBLICATIONS

Bennouna J et al. **Continuation of bevacizumab after first progression in metastatic colorectal cancer (ML18147): A randomised phase 3 trial.** *Lancet Oncol* 2013;14(1):29-37.

Chen L-T 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**.

Ferry D et al. **On-treatment progression-free survival analysis of ziv-aflibercept/FOLFIRI treatment within 28 days of end of treatment in metastatic colorectal cancer: Updated efficacy results from the VELOUR study.** *Proc ASCO* 2013;**Abstract 3573**.

Fuchs C et al. **Ramucirumab monotherapy for previously treated advanced gastric or gastro-oesophageal junction adenocarcinoma (REGARD): An international, randomised, multicentre, placebo-controlled, phase 3 trial.** *Lancet* 2014;383(9911):31-9.

Gibbs P et al. **Selective Internal Radiation Therapy (SIRT) with yttrium-90 resin microspheres plus standard systemic chemotherapy regimen of FOLFOX versus FOLFOX alone as first-line treatment of non-resectable liver metastases from colorectal cancer: The SIRFLOX study.** *BMC Cancer* 2014;14:897.

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.

Hitron M et al. **A phase 1b study of the cancer stem cell inhibitor BBI608 administered with paclitaxel in patients with advanced malignancies.** *Proc ASCO* 2014;**Abstract 2530**.

Hurwitz H et al. **A randomized double-blind phase 2 study of ruxolitinib (RUX) or placebo (PBO) with capecitabine (CAPE) as second-line therapy in patients (pts) with metastatic pancreatic cancer (mPC).** *Proc ASCO* 2014;**Abstract 4000**.

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.

Kim T et al. **CONCUR: A randomized, placebo-controlled phase 3 study of regorafenib (REG) monotherapy in Asian patients with previously treated metastatic colorectal cancer (mCRC).** *Proc ESMO* 2014;**Abstract 500O**.

Kubicka S et al. **Bevacizumab plus chemotherapy continued beyond first progression in patients with metastatic colorectal cancer previously treated with bevacizumab plus chemotherapy: ML18147 study KRAS subgroup findings.** *Ann Oncol* 2013;24(9):2342-9.

Martin LK et al. **Yttrium-90 radioembolization as salvage therapy for colorectal cancer with liver metastases.** *Clin Colorectal Cancer* 2012;11(3):195-9.

Muro K et al. **Relationship between PD-L1 expression and clinical outcomes in patients (Pts) 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**.

Peeters M et al. **Final results from a randomized phase 3 study of FOLFIRI {+/-} panitumumab for second-line treatment of metastatic colorectal cancer.** *Ann Oncol* 2014;25(1):107-16.

Ruff P et al. **Analysis of overall survival and safety during the course of the phase III VELOUR trial comparing FOLFIRI and ziv-aflibercept or placebo in mCRC patients who progressed on prior oxaliplatin treatment.** *Proc ASCO* 2013;**Abstract 3574**.

Tabernero J et al. **RAISE: A randomized, double-blind, multicenter phase III study of irinotecan, folinic acid, and 5-fluorouracil (FOLFIRI) plus ramucirumab (RAM) or placebo (PBO) in patients (pts) with metastatic colorectal carcinoma (CRC) progressive during or following first-line combination therapy with bevacizumab (bev), oxaliplatin (ox), and a fluoropyrimidine (fp).** Gastrointestinal Cancers Symposium 2015;**Abstract 512**.

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.

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.

Yoon H et al. **Ramucirumab (RAM) plus FOLFOX as front-line therapy (Rx) for advanced gastric or esophageal adenocarcinoma (GE-AC): Randomized, double-blind, multicenter phase 2 trial.** *Proc ASCO* 2014;**Abstract 4004**.

Yoshino T et al. **TAS-102 monotherapy for pretreated metastatic colorectal cancer: A double-blind, randomised, placebo-controlled phase 2 trial.** *Lancet Oncol* 2012;13(10):993-1001.

Yoshino Y et al. **Results of a multicenter, randomised, double-blind, phase III study of TAS-102 vs placebo, with best supportive care (BSC), in patients with metastatic colorectal cancer (mCRC) refractory to standard therapies (RECOURSE).** *Proc ESMO* WCGC 2014;**Abstract O-0022**.

POST-TEST

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QUESTIONS (PLEASE CIRCLE ANSWER):

1. **The RAINBOW trial of paclitaxel with or without ramucirumab for patients with metastatic gastric or gastroesophageal junction adenocarcinoma after disease progression on first-line therapy demonstrated a statistically significant benefit in _____ with the addition of ramucirumab.**
   a. Overall survival
   b. Progression-free survival
   c. Objective response rate
   d. All of the above

2. **What was the most common Grade 3 or higher adverse event associated with TAS-102 in the Phase III RECOURSE study for patients with metastatic CRC that is refractory to standard therapies?**
   a. Neutropenia
   b. Diarrhea
   c. Hand-foot syndrome

3. **Which of the following were the most problematic toxicities of regorafenib in the 2 Phase III studies (CORRECT and CONCUR) that demonstrated significant benefits with regorafenib versus placebo in the third-line setting for patients with metastatic CRC?**
   a. Myalgia
   b. Hand-foot syndrome and fatigue
   c. Anemia
   d. None of the above

4. **The Phase II ReDOS study is designed to compare initial dosing of regorafenib at 160 mg/day versus _____ in patients with refractory metastatic CRC.**
   a. 120 mg/day
   b. 80 mg/day
   c. Weekly dose escalation from 80 to 160 mg/day

5. **What were the preliminary results from the Phase III SIRFLOX study evaluating FOLFOX with or without Y-90 resin microspheres as first-line treatment for metastatic CRC with unresectable liver metastases with or without limited extrahepatic disease?**
   a. Improvement in progression-free survival in the overall population
   b. Improvement in progression-free survival in the liver
   c. Improvement in overall survival
   d. None of the above

6. **The Phase III NAPOLI-1 trial demonstrated statistically significant improvements in progression-free and overall survival with the combination of _____ and 5-FU/LV versus 5-FU/LV alone for patients with metastatic pancreatic cancer after gemcitabine-based therapy.**
   a. Ruxolitinib
   b. Liposomal irinotecan (MM-398)
   c. BBI608

7. **The randomized, double-blind Phase II RECAP study of ruxolitinib or placebo with capecitabine as second-line therapy for patients with metastatic pancreatic cancer demonstrated an overall survival benefit with ruxolitinib in patients who had a serum C-reactive protein level of greater than 13 mg/L.**
   a. True
   b. False

8. **_____ is a novel cancer stem cell inhibitor that has shown promising activity in early studies for patients with advanced gastric cancer.**
   a. Ruxolitinib
   b. Pembrolizumab
   c. BBI608

EDUCATIONAL ASSESSMENT AND CREDIT FORM

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Research To Practice is committed to providing valuable continuing education for oncology clinicians, and your input is critical to helping us achieve this important goal. Please take the time to assess the activity you just completed, with the assurance that your answers and suggestions are strictly confidential.

PART 1 — Please tell us about your experience with this educational activity

How would you characterize your level of knowledge on the following topics?

4 = Excellent 3 = Good 2 = Adequate 1 = Suboptimal

	BEFORE	AFTER
Efficacy of ruxolitinib in combination with capecitabine for metastatic pancreatic cancer	4 3 2 1	4 3 2 1
Mechanism of action of TAS-102 and results of the Phase III RECOURSE study in patients with metastatic CRC	4 3 2 1	4 3 2 1
Results of the Phase III RAISE study of ramucirumab in combination with FOLFIRI for metastatic CRC	4 3 2 1	4 3 2 1
Clinical strategies to prevent and manage regorafenib-associated side effects	4 3 2 1	4 3 2 1
Early data with cancer stem cell and checkpoint inhibitors for advanced gastric cancer	4 3 2 1	4 3 2 1

Practice Setting:

☐ Academic center/medical school ☐ Community cancer center/hospital ☐ Group practice
☐ Solo practice ☐ Government (eg, VA) ☐ Other (please specify).....

Approximately how many new patients with colorectal, gastric and pancreatic cancer do you see per year? Colorectal:..... Gastric:..... Pancreatic:.....

Was the activity evidence based, fair, balanced and free from commercial bias?

☐ Yes ☐ No If no, please explain:.....

Please identify how you will change your practice as a result of completing this activity (select all that apply).

☐ This activity validated my current practice
☐ Create/revise protocols, policies and/or procedures
☐ Change the management and/or treatment of my patients
☐ Other (please explain):.....

If you intend to implement any changes in your practice, please provide 1 or more examples:

.....

The content of this activity matched my current (or potential) scope of practice.

☐ Yes ☐ No If no, please explain:.....

Please respond to the following learning objectives (LOs) by circling the appropriate selection:

4 = Yes 3 = Will consider 2 = No 1 = Already doing N/M = LO not met N/A = Not applicable

As a result of this activity, I will be able to:

- Effectively apply the results of practice-changing clinical research to the selection and sequencing of chemobiologic regimens for patients with metastatic CRC..... 4 3 2 1 N/M N/A
- Educate patients with metastatic gastric or pancreatic cancer regarding approved and novel treatment approaches and their associated risks and benefits..... 4 3 2 1 N/M N/A
- Appreciate the recent FDA-approved indications for ramucirumab alone or in combination with paclitaxel for advanced gastric or gastroesophageal junction cancer, and discern how this agent can be optimally integrated into clinical practice..... 4 3 2 1 N/M N/A
- Implement a clinical plan for the management of advanced HER2-positive gastric cancer, incorporating existing and emerging treatments..... 4 3 2 1 N/M N/A
- Recall new data with investigational agents demonstrating promising activity in colorectal, gastric and pancreatic cancers..... 4 3 2 1 N/M N/A

EDUCATIONAL ASSESSMENT AND CREDIT FORM (continued)

Please describe any clinical situations that you find difficult to manage or resolve that you would like to see addressed in future educational activities:

.....

Would you recommend this activity to a colleague?

☐ Yes ☐ No

If no, please explain:.....

Additional comments about this activity:

.....

As part of our ongoing, continuous quality-improvement effort, we conduct postactivity follow-up surveys to assess the impact of our educational interventions on professional practice. Please indicate your willingness to participate in such a survey.

☐ Yes, I am willing to participate in a follow-up survey.

☐ No, I am not willing to participate in a follow-up survey.

PART 2 — Please tell us about the faculty and editor for this educational activity

4 = Excellent 3 = Good 2 = Adequate 1 = Suboptimal

Faculty	Knowledge of subject matter	Effectiveness as an educator
Philip A Philip, MD, PhD	4 3 2 1	4 3 2 1
Tanios Bekaii-Saab, MD	4 3 2 1	4 3 2 1
Editor	**Knowledge of subject matter**	**Effectiveness as an educator**
Neil Love, MD	4 3 2 1	4 3 2 1

Please recommend additional faculty for future activities:

.....

Other comments about the faculty and editor for this activity:

.....

.....

REQUEST FOR CREDIT — Please print clearly

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Professional Designation:

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I certify my actual time spent to complete this educational activity to be _____ hour(s).

Signature:..... Date:.....

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