GASTROINTESTINAL CANCER TUMOR PANEL

Clinical Investigators Provide Their Perspectives on Current Cases and Clinical Issues in the Management of Colorectal, Gastric and Pancreatic Cancer

Faculty Interviews

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From the publishers of:

Gastrointestinal Cancer™ UPDATE

CME Certified

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Gastrointestinal Cancer Tumor Panel: *Clinical Investigators Provide Their Perspectives on Current Cases and Clinical Issues in the Management of 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) 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

- Communicate the benefits and risks of approved anti-VEGF and other targeted biologic therapies to patients with metastatic CRC, and develop an evidence-based algorithm to sequence these 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.
- Implement a clinical plan for the management of advanced HER2-positive gastric cancer, incorporating existing and emerging targeted treatments.
- Appreciate available clinical research data documenting the efficacy of ramucirumab in advanced gastric or gastro-esophageal junction cancer, and discern how this agent can be optimally integrated into clinical practice for patients with HER2-negative and HER2-positive disease.
- 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 proposed mechanism of action and available research data with ruxolitinib in pancreatic cancer, and use this information to counsel appropriate patients regarding ongoing trials evaluating this novel approach.

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CME INFORMATION

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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: **Dr Grothey** — Contracted Research: Bayer HealthCare Pharmaceuticals, Eisai Inc, Genentech BioOncology, Lilly, Pfizer Inc, Sanofi. **Dr O'Reilly** — Consulting Agreements: Abbott Laboratories, Aduro Biotech, Amgen Inc, Astellas Scientific and Medical Affairs Inc, Celgene Corporation, Celsion Corporation, Chugai Pharmaceutical Co Ltd, Cipla Ltd, EntreMed Inc, Exelixis Inc, Genentech BioOncology, Gilead Sciences Inc, ImClone Systems, a wholly owned subsidiary of Eli Lilly and Company, IntegraGen, Jennerex Inc, Lilly, MedImmune Inc, Momenta Pharmaceuticals Inc, Novartis Pharmaceuticals Corporation, Roche Laboratories Inc, Sanofi, Silenseed Ltd, Vicus Therapeutics; Contracted Research: Abbott Laboratories, Amgen Inc, AstraZeneca Pharmaceuticals LP, Bayer HealthCare Pharmaceuticals, Exelixis Inc, Genentech BioOncology, ImClone Systems, a wholly owned subsidiary of Eli Lilly and Company, Momenta Pharmaceuticals Inc, Myriad Genetic Laboratories Inc, Novartis Pharmaceuticals Corporation, OncoMed Pharmaceuticals Inc, Onyx Pharmaceuticals, an Amgen subsidiary, Polaris Group, Roche Laboratories Inc, Vicus Therapeutics.

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SELECT PUBLICATIONS

A randomized, double-blind, phase 3 study of the JAK 1/2 inhibitor, ruxolitinib or placebo in combination with capecitabine in subjects with advanced or metastatic adenocarcinoma of the pancreas who have failed or are intolerant to first-line chemotherapy (the JANUS 2 study). NCT02119663

A randomized, double-blind, phase 3 study of the Janus kinase (JAK) 1/2 inhibitor, ruxolitinib, or placebo in combination with capecitabine in subjects with advanced or metastatic adenocarcinoma of the pancreas who have failed or are intolerant to first-line chemotherapy (the JANUS 1 study). NCT02117479

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Mayer RJ et al. **Randomized trial of TAS-102 for refractory metastatic colorectal cancer.** *N Engl J Med* 2015;372(20):1909-19.

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Tabernero J et al. **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(6):e262.

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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.

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POST-TEST

Gastrointestinal Tumor Panel: *Clinical Investigators Provide Their Perspectives on Current Cases and Clinical Issues in the Management of Colorectal, Gastric and Pancreatic Cancer*

QUESTIONS (PLEASE CIRCLE ANSWER):

1. **Analysis of the N9741 trial comparing first-line FOLFOX to irinotecan-containing regimens for patients with metastatic CRC demonstrated that the "sweet spot" for achieving optimal response while minimizing Grade 3 neurotoxicity was observed after how many cycles (cumulative dose) of oxaliplatin?**
   a. 10 cycles (850 mg/m^2)
   b. 8 cycles (680 mg/m^2)
   c. 6 cycles (510 mg/m^2)

2. **A recent study published in *The New England Journal of Medicine* demonstrated that 40% of patients with mismatch repair-deficient colorectal tumors responded to pembrolizumab.**
   a. True
   b. False

3. **In the HERACLES study, patients with KRAS wild-type, HER2-amplifed, refractory (median of 5 prior treatments) metastatic CRC treated with trastuzumab and lapatinib achieved an overall response rate of 35% and a disease control rate of 78%.**
   a. True
   b. False

4. **When do the most common regorafenib-associated side effects tend to occur in patients with metastatic CRC?**
   a. In later cycles, as a cumulative effect of treatment
   b. Early, during the first cycle
   c. Neither, the timing of side effects is completely unpredictable

5. **Which of the following is true when initiating regorafenib at 160 mg/day for a patient with metastatic CRC?**
   a. The majority of patients will require dose adjustments
   b. The majority of patients will tolerate the dose well, without significant side effects
   c. 160 mg/day is higher than the package insert dose and should not be administered

6. **Which of the following is the primary dose-limiting toxicity associated with TAS-102?**
   a. Diarrhea
   b. Hand-foot syndrome
   c. Neutropenia
   d. None of the above

7. **Which of the following is a key eligibility criterion for the Phase III JANUS 1 and 2 studies evaluating capecitabine and ruxolitinib in patients with advanced or metastatic pancreatic cancer?**
   a. No prior treatment for advanced or metastatic disease
   b. Elevated C-reactive protein
   c. Both a and b

8. **The Phase III RAINBOW trial evaluating ramucirumab with paclitaxel versus placebo with paclitaxel demonstrated a(n) _____ benefit with the addition of ramucirumab for patients with previously treated advanced gastric or gastroesophageal cancer.**
   a. Overall survival
   b. Progression-free survival
   c. Both a and b
   d. Neither a nor b

EDUCATIONAL ASSESSMENT AND CREDIT FORM

Gastrointestinal Cancer Tumor Panel: *Clinical Investigators Provide Their Perspectives on Current Cases and Clinical Issues in the Management of Colorectal, Gastric and Pancreatic Cancer*

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
Correlation between mismatch repair status and benefit from immune checkpoint blockade	4 3 2 1	4 3 2 1
Initial dosing and time to onset of regorafenib-associated side effects	4 3 2 1	4 3 2 1
RECOURSE: Tolerability and survival benefit of TAS-102 in refractory, metastatic CRC	4 3 2 1	4 3 2 1
HERACLES: Activity of trastuzumab/lapatinib in HER2-amplified metastatic CRC	4 3 2 1	4 3 2 1
Role of ramucirumab in patients with HER2-positive metastatic gastric cancer	4 3 2 1	4 3 2 1
Rationale for and design of ongoing Phase III Janus 1 and Janus 2 trials evaluating the role of ruxolitinib with capecitabine in patients with advanced pancreatic 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:

- Communicate the benefits and risks of approved anti-VEGF and other targeted biologic therapies to patients with metastatic CRC, and develop an evidence-based algorithm to sequence these available options based on disease- and patient-specific characteristics..... 4 3 2 1 N/M N/A
- Individualize local and systemic treatment for patients with metastatic CRC that is isolated to the liver..... 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 targeted treatments..... 4 3 2 1 N/M N/A

EDUCATIONAL ASSESSMENT AND CREDIT FORM (continued)

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

- Appreciate available clinical research data documenting the efficacy of 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. . . . . 4 3 2 1 N/M N/A
- Appraise the rationale for and clinical data with investigational anti-PD-1 and/or anti-PD-L1 antibodies in patients with gastric cancer. . . . . 4 3 2 1 N/M N/A
- Consider age, performance status and other clinical factors in the selection of systemic therapy for patients with metastatic pancreatic adenocarcinoma. . . . . 4 3 2 1 N/M N/A
- Describe the proposed mechanism of action and available research data with ruxolitinib in pancreatic cancer, and use this information to counsel appropriate patients regarding ongoing trials evaluating this novel approach. . . . . 4 3 2 1 N/M N/A

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: .....

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
Axel Grothey, MD	4 3 2 1	4 3 2 1
Eileen M O'Reilly, 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:

.....

REQUEST FOR CREDIT — Please print clearly

Name: ..... Specialty: .....

Professional Designation:

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

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Gastrointestinal Cancer™

U P D A T E

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