

Novel Agents and Emerging Strategies in the Management of Metastatic Colorectal Cancer

A Special Edition Interview Program

FACULTY INTERVIEWS

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CME
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Novel Agents and Emerging Strategies in the Management of Metastatic Colorectal Cancer

A Continuing Medical Education Audio Program

OVERVIEW OF ACTIVITY

Metastatic colorectal cancer (mCRC) is a common and often lethal condition, and its clinical management is constantly evolving. As published results from ongoing trials lead to the emergence of novel biomarkers and new therapeutic targets and regimens, existing treatment algorithms may be altered. 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. To bridge the gap between research and patient care, this special edition interview program uses one-on-one discussion with 2 leading gastrointestinal oncology investigators. By providing access to the latest scientific developments and the perspectives of experts in the field, this CME activity assists medical oncologists with the formulation of up-to-date management strategies.

LEARNING OBJECTIVES

- Coordinate comprehensive biomarker analysis for patients diagnosed with mCRC, and use this information to guide evidence-based care for these patients.
- Communicate the benefits and risks of approved anti-VEGF, anti-EGFR and other targeted biologic therapies to patients with mCRC, and develop an evidence-based algorithm to sequence available options based on disease- and patient-specific characteristics.
- Understand practical considerations surrounding the use of regorafenib for patients with mCRC to ensure appropriate administration and patient safety.
- Assess the potential role of anti-PD-1 antibodies in the treatment of mCRC.
- Counsel appropriately selected patients with mCRC about participation in ongoing clinical trials.

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HOW TO USE THIS CME ACTIVITY

This CME activity contains an audio component. To receive credit, the participant should review the CME information, listen to the CD and bonus web-only audio, complete the Post-test with a score of 75% or better and fill out the Educational Assessment and Credit Form located in the back of this booklet or on our website at ResearchToPractice.com/MCRC115/CME. A complete list of supporting references may also be accessed at ResearchToPractice.com/MCRC115.

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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: **Dr Marshall** — Advisory Committee: Amgen Inc, Bayer HealthCare Pharmaceuticals, Boehringer Ingelheim Pharmaceuticals Inc, Celgene Corporation, Daiichi Sankyo Inc, Genentech BioOncology; Consulting Agreements, Contracted Research and Speakers Bureau: Amgen Inc, Bayer HealthCare Pharmaceuticals, Celgene Corporation, Genentech BioOncology. **Prof Van Cutsem** — Consulting Agreements: Bayer HealthCare Pharmaceuticals, Lilly; Research Grant: Amgen Inc, Bayer HealthCare Pharmaceuticals, Boehringer Ingelheim Pharmaceuticals Inc, Merck Serono, Novartis Pharmaceuticals Corporation, Roche Laboratories Inc, Sanofi.

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SELECT PUBLICATIONS

Atreya CE et al. **Updated efficacy of the MEK inhibitor trametinib (T), BRAF inhibitor dabrafenib (D), and anti-EGFR antibody panitumumab (P) in patients (pts) with BRAF V600E mutated (BRAFM) metastatic colorectal cancer (mCRC).** *Proc ASCO* 2015;Abstract 103.

Cleary JM et al. **Population pharmacokinetic (PK) analysis of TAS-102 in patients (pts) with metastatic colorectal cancer (mCRC): Results from 3 phase 1 trials and the phase 3 RECOURSE trial.** *Proc ASCO* 2015;Abstract 2579.

Fu AZ et al. **Utilization of bevacizumab in US elderly patients with colorectal cancer receiving chemotherapy.** *J Oncol Pharm Pract* 2014;20(5):332-40.

Lai S et al. **Rechallenging 5-fluorouracil in a patient with capecitabine-induced ventricular fibrillation.** *Clin Colorectal Cancer* 2015;14(3):198-201.

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Loupakis F et al. **FOLFOXIRI plus bevacizumab as first-line treatment in BRAF mutant metastatic colorectal cancer.** *Eur J Cancer* 2014;50(1):57-63.

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Ruff P et al. **Time course of safety and efficacy of aflibercept in combination with FOLFIRI in patients with metastatic colorectal cancer who progressed on previous oxaliplatin-based therapy.** *Eur J Cancer* 2015;51(1):18-26.

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Sun JF et al. **Safety of chronic low-dose capecitabine as maintenance therapy in gastrointestinal cancers.** *Gastrointest Cancer Res* 2009;3(4):134-40.

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. **Results from the large, open-label phase 3b CONSIGN study of regorafenib in patients with previously treated metastatic colorectal cancer.** ESMO World Congress on Gastrointestinal Cancer 2015;Abstract LBA-05.

Van Cutsem E et al. **TAS-102 vs placebo (PBO) in patients (pts) ≥65 years (y) with metastatic colorectal cancer (mCRC): An age-based analysis.** *Proc ASCO* 2015;Abstract 3595.

Van Cutsem E et al. **Updated results of the MEK inhibitor trametinib (T), BRAF inhibitor dabrafenib (D), and anti-EGFR antibody panitumumab (P) in patients (pts) with BR.** ESMO World Congress on Gastrointestinal Cancer 2015;Abstract LBA-07.

Van Cutsem E et al, on behalf of the ESMO Guidelines Working Group. **Metastatic colorectal cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up.** *Ann Oncol* 2014;25(Suppl 3):iii1-9.

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QUESTIONS (PLEASE CIRCLE ANSWER):

1. A study presented at ASCO 2015 investigating the association between plasma vitamin D levels and survival in patients with mCRC enrolled on the CALGB-80405 trial demonstrated that higher vitamin D levels do not correlate with improved overall survival.
 - a. True
 - b. False
2. Patients with BRAF-mutant mCRC _____.
 - a. Have a poor prognosis
 - b. Do not benefit significantly with BRAF inhibitors alone in late-line therapy
 - c. Both a and b
3. A study investigating the efficacy of immune checkpoint inhibition with pembrolizumab according to DNA mismatch repair status in patients with metastatic carcinoma demonstrated dramatic responses in patients with mismatch repair-deficient tumors.
 - a. True
 - b. False
4. Adverse events associated with the oral nucleoside TAS-102 include _____.
 - a. Neutropenia
 - b. Fatigue
 - c. Deep vein thrombosis
 - d. Both a and b
 - e. All of the above
5. ESMO clinical practice guidelines recommend genomic testing for _____ in patients with mCRC.
 - a. RAS mutations
 - b. BRAF mutations
 - c. Both a and b
6. The incidence of BRAF mutations in patients with CRC is _____.
 - a. Less than 15%
 - b. Approximately 50%
 - c. 60% to 80%
7. Which of the following statements is true regarding the toxicity associated with regorafenib?
 - a. Dose reduction can be used to mitigate adverse events
 - b. The most severe side effects are observed in later cycles
 - c. Severe side effects include hand-foot reaction, fatigue and diarrhea
 - d. Both a and c
 - e. All of the above
8. Which of the following appears to be true from cross-trial comparison of anti-angiogenic agents in mCRC?
 - a. Bevacizumab is more active than aflibercept and ramucirumab
 - b. Aflibercept is more active than bevacizumab and ramucirumab
 - c. Ramucirumab is more active than bevacizumab and aflibercept
 - d. All have similar activity

EDUCATIONAL ASSESSMENT AND CREDIT FORM

Novel Agents and Emerging Strategies in the Management of Metastatic Colorectal 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 DNA mismatch repair status and benefit from immune checkpoint blockade in mCRC	4 3 2 1	4 3 2 1
Activity and tolerability of ramucirumab as second-line therapy for mCRC	4 3 2 1	4 3 2 1
Results of the Phase III CONSIGN study of regorafenib for patients with previously treated mCRC	4 3 2 1	4 3 2 1
Correlation between central tumor necrosis observed radiographically and benefit from regorafenib	4 3 2 1	4 3 2 1
Available data with TAS-102 and current integration into the management of mCRC	4 3 2 1	4 3 2 1
Efficacy of BRAF/MEK inhibitors in combination with anti-EGFR antibodies for BRAF mutation-positive mCRC	4 3 2 1	4 3 2 1
ESMO clinical practice guidelines for patients with mCRC	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 CRC do you see per year? patients

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:

- Coordinate comprehensive biomarker analysis for patients diagnosed with mCRC, and use this information to guide evidence-based care for these patients..... 4 3 2 1 N/M N/A
- Communicate the benefits and risks of approved anti-VEGF, anti-EGFR and other targeted biologic therapies to patients with mCRC, and develop an evidence-based algorithm to sequence available options based on disease- and patient-specific characteristics 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:

- Understand practical considerations surrounding the use of regorafenib for patients with mCRC to ensure appropriate administration and patient safety. . . . 4 3 2 1 N/M N/A
- Assess the potential role of anti-PD-1 antibodies in the treatment of mCRC. . . . 4 3 2 1 N/M N/A
- Counsel appropriately selected patients with mCRC about participation in ongoing clinical trials. . . . 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:

Additional comments about this activity:

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

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Faculty	Knowledge of subject matter			Effectiveness as an educator
John L Marshall, MD	4	3	2	1
Eric Van Cutsem, MD, PhD	4	3	2	1
Editor	Knowledge of subject matter			Effectiveness as an educator
Neil Love, MD	4	3	2	1

Please recommend additional faculty for future activities:

Other comments about the faculty and editor for this activity:

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