VOL 9 | ISSUE 1

Colorectal Cancer™ UPDATE

Conversations with Oncology Investigators

Bridging the Gap between Research and Patient Care

FACULTY INTERVIEWS

Alan P Venook, MD
Scott Kopetz, MD, PhD
Zev Wainberg, MD, MSc
Howard S Hochster, MD

EDITOR

Neil Love, MD

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2 Audio CDs

Colorectal Cancer Update

A Continuing Medical Education Audio Series

OVERVIEW OF ACTIVITY

Approximately 135,000 people were diagnosed with colon or rectal cancer in the United States in 2017 alone, with nearly 50,000 of these individuals succumbing to their disease. Published results from ongoing trials continually lead to the emergence of new therapeutic targets and regimens, thereby altering existing management algorithms. 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, *Colorectal Cancer Update* uses one-on-one discussion with 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

- Formulate an individualized approach to the selection of adjuvant chemotherapy regimens and the duration of treatment for patients with standard- and high-risk colon cancer.
- Consider patient and disease characteristics in selecting therapy for patients with metastatic colorectal cancer (mCRC), including primary tumor location and presence of potentially targetable genetic abnormalities (eg, BRAF, HER2).
- Appraise the recent approvals of pembrolizumab and nivolumab for patients with microsatellite instability-high or mismatch repair-deficient tumors, and integrate these agents into current mCRC treatment algorithms.
- Devise a rational approach to the incorporation of regorafenib and TAS-102 into the treatment algorithm for mCRC that includes consideration of each agent's unique side-effect profile.
- Counsel patients regarding the incidence and manifestation of side effects associated with commonly used systemic agents and regimens, and develop a plan to optimally manage these toxicities.
- Recall available and emerging data with other investigational agents currently being tested in clinical trials for CRC, and refer eligible patients for trial participation or expanded access programs.

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EDITOR

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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 Venook** — Advisory Committee: Bayer HealthCare Pharmaceuticals, Genentech BioOncology; Contracted Research: Bristol-Myers Squibb Company, Genentech BioOncology, Merck, Taiho Oncology Inc. **Dr Kopetz** — Consulting Agreements: Amgen Inc, Bayer HealthCare Pharmaceuticals, Genentech BioOncology. **Dr Wainberg** — Advisory Committee: Genentech BioOncology, Lilly, Merck, Novartis; Contracted Research: Bristol-Myers Squibb Company, Celgene Corporation, Genentech BioOncology, Lilly, Merck, Novartis. **Dr Hochster** — Consulting Agreements: Bayer HealthCare Pharmaceuticals, Bristol-Myers Squibb Company, Genomic Health Inc.

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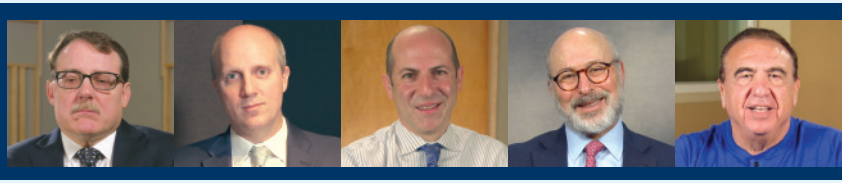
Video Program

View the corresponding video interviews with (from left) Drs Venook, Kopetz, Wainberg and Hochster by Dr Love www.ResearchToPractice.com/CCU118/Video



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Sundar R et al. **Targeting *BRAF*-mutant colorectal cancer: Progress in combination strategies.** *Cancer Discov* 2017;7(6):558-60.

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QUESTIONS (PLEASE CIRCLE ANSWER):

1. **The IDEA pooled analysis of studies evaluating the duration of adjuvant oxaliplatin-based therapy for patients with Stage III colon cancer demonstrated that survival outcomes were not inferior for patients with lower-risk disease who received 3 months compared to 6 months of therapy.**
   a. True
   b. False

2. **Which of the following patients with mCRC do not derive clinical benefit from the addition of EGFR antibodies to first-line chemotherapy?**
   a. Patients with left-sided primary cancers
   b. Patients with right-sided primary cancers

3. **Approximately what proportion of patients with CRC have HER2-amplifed or HER2-mutated disease?**
   a. 20%
   b. 10%
   c. 4%

4. **In the randomized Phase II SWOG-S1613 study, which nonchemotherapy-containing HER2-targeted doublet will be compared to cetuximab/irinotecan for HER2-amplified mCRC?**
   a. T-DM1/lapatinib
   b. Trastuzumab/lapatinib
   c. Trastuzumab/pertuzumab

5. **Which of the following phenotypes tends to be associated with MSI-high colon cancer?**
   a. Right sidedness
   b. Mucinous type
   c. BRAF mutation
   d. All of the above

6. **What was the response rate in the CheckMate 142 study of single-agent nivolumab for previously treated MSI-high or mismatch repair-deficient mCRC?**
   a. 50%
   b. 25%
   c. 10%

7. **Both pembrolizumab and nivolumab are indicated for the treatment of metastatic MSI-high or mismatch repair-deficient CRC that progresses after previous therapy.**
   a. True
   b. False

8. **In patients with MSI-high CRC the mutational load is _____ compared to the mutational load in patients with MSS CRC.**
   a. Approximately 100 times higher
   b. Roughly equivalent
   c. Lower

9. **Which of the following results was observed in the SWOG-S1406 study with the addition of vemurafenib to cetuximab/irinotecan for patients with treatment-refractory BRAF V600E-mutated mCRC?**
   a. Doubling of progression-free survival
   b. Tripling of the disease control rate
   c. Significant increase in skin toxicity
   d. All of the above
   e. Both a and b

10. **The onset and delayed recovery of neutropenia has been demonstrated to be a positive predictive factor for outcomes with TAS-102 treatment.**
    a. True
    b. False

EDUCATIONAL ASSESSMENT AND CREDIT FORM

Colorectal Cancer Update — Volume 9, Issue 1

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
IDEA pooled analysis evaluating the duration of adjuvant oxaliplatin-based chemotherapy for Stage III colon cancer	4 3 2 1	4 3 2 1
Clinical trial data with and indications for anti-PD-1 checkpoint inhibitors in the treatment of MSI-high or mismatch repair-deficient mCRC	4 3 2 1	4 3 2 1
SWOG-S1406 trial: Efficacy and tolerability of irinotecan/cetuximab and vemurafenib for BRAF-mutated mCRC	4 3 2 1	4 3 2 1
Strategies based on side-effect profiles for sequencing TAS-102 and regorafenib for mCRC	4 3 2 1	4 3 2 1
Ongoing Alliance A021502 Phase III study of adjuvant chemotherapy alone or combined with atezolizumab for Stage III colon cancer with deficient DNA mismatch repair	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 cancer do you see per year? .....

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:

- Formulate an individualized approach to the selection of adjuvant chemotherapy regimens and the duration of treatment for patients with standard- and high-risk colon cancer. .....4 3 2 1 N/M N/A
- Consider patient and disease characteristics in selecting therapy for patients with metastatic colorectal cancer (mCRC), including primary tumor location and presence of potentially targetable genetic abnormalities (eg, BRAF, HER2). .....4 3 2 1 N/M N/A
- Appraise the recent approvals of pembrolizumab and nivolumab for patients with microsatellite instability-high or mismatch repair-deficient tumors, and integrate these agents into current mCRC treatment algorithms. .....4 3 2 1 N/M N/A
- Devise a rational approach to the incorporation of regorafenib and TAS-102 into the treatment algorithm for mCRC that includes consideration of each agent's unique side-effect profile. .....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:

- Counsel patients regarding the incidence and manifestation of side effects associated with commonly used systemic agents and regimens, and develop a plan to optimally manage these toxicities. . . . . 4 3 2 1 N/M N/A
- Recall available and emerging data with other investigational agents currently being tested in clinical trials for CRC, and refer eligible patients for trial participation or expanded access programs. . . . . 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**
Alan P Venook, MD	4 3 2 1	4 3 2 1
Scott Kopetz, MD, PhD	4 3 2 1	4 3 2 1
Zev Wainberg, MD, MSc	4 3 2 1	4 3 2 1
Howard S Hochster, 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

REQUEST FOR CREDIT — Please print clearly

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