Colorectal Cancer

U P D A T E

Conversations with Oncology Investigators Bridging the Gap between Research and Patient Care

MODERATOR

Neil Love. MD

CO-CHAIR

Richard M Goldberg, MD

FACULTY

Jordan D Berlin, MD Lee M Ellis, MD Charles S Fuchs, MD, MPH Axel Grothey, MD

SPECIAL ISSUE

Proceedings from a Clinical Investigator Think Tank

> Daniel G Haller, MD Herbert I Hurwitz, MD Neal J Meropol, MD Alan P Venook, MD









Colorectal Cancer Update

A Continuing Medical Education Audio Series

OVERVIEW OF ACTIVITY

Colorectal cancer is among the most common types of cancer in the United States, and the treatment of this disease continues to evolve. Published results from ongoing clinical trials lead to the emergence of new therapeutic agents and regimens, changes in the indications, doses and schedules for existing treatments and the development of new genomic assays and markers with prognostic and/or predictive potential. 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. By providing access to the latest research developments and expert perspectives, this CME activity assists medical oncologists in the formulation of up-to-date clinical management strategies.

LEARNING OBJECTIVES

- Utilize assessment of K-ras mutation status to select appropriate patients with colorectal cancer (CRC) who may benefit from treatment with EGFR inhibitors.
- Develop an evidence-based algorithm for the treatment of metastatic CRC that incorporates the individualized
 use of bevacizumab, cetuximab and other biologic agents based on an understanding of their unique efficacy and
 tolerability profiles.
- Appraise the clinical value of continuing therapy with biologic agents beyond initial disease progression.
- Recognize patients with isolated CRC hepatic metastases who may be eligible for surgical cure, considering the utility
 of conversion therapy and perioperative/postoperative systemic treatments.
- Describe existing and investigational biomarkers used to predict risk of CRC recurrence and/or response to targeted therapy.
- Identify the clinical and molecular characteristics of hereditary nonpolyposis CRC, and refer patients at high risk for genetic evaluation.
- Compare and contrast the clinical indications for preoperative and/or postoperative concomitant chemoradiation therapy among patients with locally advanced rectal cancer.
- Summarize the efficacy and toxicity findings from clinical research combining molecularly targeted agents for the treatment of advanced CRC.
- Counsel appropriately selected patients with CRC about availability of and participation in ongoing clinical trials.

ACCREDITATION STATEMENT

Research To Practice is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

CREDIT DESIGNATION STATEMENT

Research To Practice designates this educational activity for a maximum of 2.75 AMA PRA Category 1 CreditsTM. Physicians should only claim credit commensurate with the extent of their participation in the activity.

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 CDs and complete the Post-test and Educational Assessment and Credit Form located in the back of this booklet or on our website at **ResearchToPractice.com/CCU/ThinkTank**.

This program is supported by educational grants from AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Genentech BioOncology, Genomic Health Inc and ImClone Systems Incorporated.

Last review date: December 2008; Release date: December 2008; Expiration date: December 2009

If you would like to discontinue your complimentary subscription to *Colorectal Cancer Update*, please email us at Info@ResearchToPractice.com, call us at (800) 648-8654 or fax us at (305) 377-9998. Please include your full name and address, and we will remove you from the mailing list.

CONTENT VALIDATION AND DISCLOSURES

Research To Practice (RTP) is committed to providing its participants with high-quality, unbiased and state-of-the-art education. We assess potential conflicts of interest with faculty, planners and managers of CME activities. Real or apparent conflicts of interest are identified and resolved through a conflict of interest resolution process. In addition, all activity content is reviewed by both a member of the RTP scientific staff and an external, independent physician reviewer for fair balance, scientific objectivity of studies referenced and patient care recommendations.

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 Berlin — Advisory Committee: Amgen Inc; Consulting Agreements: AstraZeneca Pharmaceuticals LP, Bayer Pharmaceuticals Corporation, Bristol-Myers Squibb Company, Genentech BioOncology, ImClone Systems Incorporated, Pfizer Inc., Sanofi-Aventis; Data and Safety Monitoring Committee: Pfizer Inc; Paid Speaker: Bayer Pharmaceuticals Corporation, Genentech BioOncology. **Dr Ellis** — Consulting Agreements: Genentech BioOncology, ImClone Systems Incorporated; Paid Research: Amgen Inc. ImClone Systems Incorporated, Sanofi-Aventis, Dr Fuchs — Advisory Committee: AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Genentech BioOncology, ImClone Systems Incorporated, Roche Laboratories Inc. Sanofi-Aventis: Speakers Bureau: Genentech BioOncology. Dr Goldberg — Consulting Agreements: Amgen Inc, AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Genentech BioOncology, Genomic Health Inc, ImClone Systems Incorporated, Novartis Pharmaceuticals Corporation, Pfizer Inc., Poniard Pharmaceuticals, Sanofi-Aventis. Dr Grothey — Advisory Committee: Genentech BioOncology, Genomic Health Inc, Pfizer Inc, Roche Laboratories Inc, Sanofi-Aventis; Consulting Agreements: Amgen Inc, Bayer Pharmaceuticals Corporation, Bristol-Myers Squibb Company, Genentech BioOncology, Roche Laboratories Inc. Dr Haller — Advisory Committee: Abraxis BioScience, Amgen Inc, Genentech BioOncology, Sanofi-Aventis; Consulting Agreement: Sanofi-Aventis. Dr Hurwitz — Consulting Agreements: Amgen Inc, Bristol-Myers Squibb Company, Genentech BioOncology, Roche Laboratories Inc; Paid Research: Amgen Inc, Bristol-Myers Squibb Company, Cephalon Inc, Genentech BioOncology, GlaxoSmithKline, ImClone Systems Incorporated, Novartis Pharmaceuticals Corporation, Pfizer Inc, Pharmion Corporation, Sanofi-Aventis. Dr Meropol Consulting Agreements: Amgen Inc, Genentech BioOncology, Genomic Health Inc, Pfizer Inc, Saladax Biomedical, Sanofi-Aventis, Zealand Pharma A/S; Lecture: Biogen Idec; Stock Ownership: Saladax Biomedical. Dr Venook — Advisory Committee: Amgen Inc, ImClone Systems Incorporated; Grant Funding: Genentech BioOncology; Paid Research: Novartis Pharmaceuticals Corporation, Pfizer Inc.

MODERATOR — Dr Love does not receive any direct remuneration from industry. Research To Practice receives funds in the form of educational grants to develop CME activities from the following commercial interests: Abraxis BioScience, AstraZeneca Pharmaceuticals LP, Aureon Laboratories Inc, Bayer Pharmaceuticals Corporation/Onyx Pharmaceuticals Inc, Biogen Idec, Bristol-Myers Squibb Company, Celgene Corporation, Eisai Inc, Eli Lilly and Company, Genentech BioOncology, Genomic Health Inc, GlaxoSmithKline, ImClone Systems Incorporated, Merck and Company Inc, Millennium Pharmaceuticals Inc, Novartis Pharmaceuticals Corporation, Ortho Biotech Products LP, OSI Oncology, Pfizer Inc, Roche Laboratories Inc, Sanofi-Aventis, Synta Pharmaceuticals Corp and Wyeth.

RESEARCH TO PRACTICE STAFF AND EXTERNAL REVIEWERS — The scientific staff and reviewers for Research To Practice have no real or apparent conflicts of interest to disclose.

This educational activity contains discussion of published and/or investigational uses of agents that are not indicated by the Food and Drug Administration. Research To Practice does not recommend the use of any agent outside of the labeled indications. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications and warnings. The opinions expressed are those of the presenters and are not to be construed as those of the publisher or grantors.

Colorectal Cancer Update — Think Tank Issue 1, 2008

QUESTIONS (PLEASE CIRCLE ANSWER):

1.	Emerging clinical trial data demonstrate that cetuximab is ineffective in patients with colorectal cancer. a. K-ras mutant b. Wild-type K-ras	6. Prospectively collected data from the BRiTE registry support the hypothesis that continued use of bevacizumab beyond disease progression is associated with an improved clinical outcome.
2.	In the PACCE study, was found with FOLFOX/bevacizumab/panitumumab compared to FOLFOX/bevacizumab. a. Inferior activity b. Excess toxicity c. Both a and b	a. True b. False 7. In a randomized Phase II trial, cediranib, an oral tyrosine kinase inhibitor, is combined with FOLFOX and compared to for previously treated metastatic colorectal cancer. a. FOLFOX only
3.	d. None of the above In CALGB-C80405, which evaluates chemotherapy in combination with cetuximab and/or bevacizumab for previously untreated metastatic colorectal cancer, the chemotherapy regimen used is	b. FOLFOX/bevacizumab c. FOLFIRI 8. Steatohepatitis, a major determinant of postoperative liver failure and wound healing complications, is most frequently associated with the use of
4.	a. FOLFOX b. FOLFIRI c. FOLFOX or FOLFIRI, at the discretion of the physician A correlation has been demonstrated betweeninduced hypersensitivity reactions and the IgE antibody. a. Bevacizumab b. Cetuximab c. Panitumumab	a. 5-FU b. Irinotecan c. Oxaliplatin 9. The preliminary safety data from
		NSABP-C-08 demonstrate that the addition of bevacizumab to adjuvant FOLFOX resulted in a significant increase in a. Gastrointestinal perforation b. Stroke c. Congestive heart failure
5.	A quantitative RT-PCR gene assay, tested in NSABP studies C-01 and C-02, was able to stratify patients with Stage II colon cancer into categories of low, intermediate and high risk for recurrence at five years. a. True b. False	d. None of the above 10. Data from a CALGB/IFL study demonstrated that microsatellite instability was predictive of benefit from adjuvant irinotecan. a. True b. False

EDUCATIONAL ASSESSMENT AND CREDIT FORM

Colorectal Cancer Update — Think Tank Issue 1, 2008

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 ONE — Please tell us about your experience with this educational activity

BEFORE completion of this activity, how would you characterize your level of knowledge on the following topics?	AFTER completion of this activity, how would you characterize your level of knowledge on the following topics?										
4 = Very good 3 = Above average 2 = Adequate 1 = Suboptimal	4 = Very good 3 = Above average 2 = Adequate 1 = Suboptimal										
Impact of K-ras mutations on response to EGFR inhibitors	Impact of K-ras mutations on response to EGFR inhibitors										
Combining biologic agents for the treatment of advanced colorectal cancer 4 3 2 1	Combining biologic agents for the treatment of advanced colorectal cancer 4 3 2 1										
Role of perioperative chemotherapy in pa-	Role of perioperative chemotherapy in pa-										
tients with resectable hepatic metastases 4 3 2 1 Continuation of biologic agents beyond	tients with resectable hepatic metastases 4 3 2 1 Continuation of biologic agents beyond										
disease progression	disease progression										
Was the activity evidence based, fair, balanced and	free from commercial bias?										
□ Yes □ No											
If no, please explain:											
Will this activity help you improve patient care?											
☐ Yes ☐ No ☐ Not applicable											
If no, please explain:											
Did the activity meet your educational needs and ex	rpectations?										
☐ Yes ☐ No											
If no, please explain:											
Please respond to the following LEARNER statemen	ts by circling the appropriate selection:										
4 = Yes $3 = Will consider$ $2 = No$ $1 = Already doing$	N/M = Learning objective not met N/A = Not applicable										
As a result of this activity, I will be able to: Utilize assessment of K-ras mutation status to select ap colorectal cancer (CRC) who may benefit from treatmer incorporates the individualized use of bevacizumab, cet agents based on an understanding of their unique effica Appraise the clinical value of continuing therapy with bir disease progression. Recognize patients with isolated CRC hepatic metastass surgical cure, considering the utility of conversion therap postoperative systemic treatments. Describe existing and investigational biomarkers used to recurrence and/or response to targeted therapy. Identify the clinical and molecular characteristics of herand refer patients at high risk for genetic evaluation. Compare and contrast the clinical indications for preoper concomitant chemoradiation therapy among patients with cetal cancer. Summarize the efficacy and toxicity findings from clinical molecularly targeted agents for the treatment of advance. Counsel appropriately selected patients with CRC about participation in ongoing clinical trials.	it with EGFR inhibitors										
What other practice changes will you make or consi	der making as a result of this activity?										
What additional information or training do you nee related topics?	d on the activity topics or other oncology-										

EDUCATIONAL ASSESSMENT AND CREDIT FORM (continued)

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.

PART TWO — Please tell us about the moderator and faculty for this educational activity

4 = Very good	3 = Above average		2 =	Adequate	1 = Suboptimal				
Faculty	Knowledge of subject matter				Effectiveness as an educator				
Jordan D Berlin, MD	4	3	2	1	4	3	2	1	
Lee M Ellis, MD	4	3	2	1	4	3	2	1	
Charles S Fuchs, MD, MPH	4	3	2	1	4	3	2	1	
Richard M Goldberg, MD	4	3	2	1	4	3	2	1	
Axel Grothey, MD	4	3	2	1	4	3	2	1	
Daniel G Haller, MD	4	3	2	1	4	3	2	1	
Herbert I Hurwitz, MD	4	3	2	1	4	3	2	1	
Neal J Meropol, MD	4	3	2	1	4	3	2	1	
Alan P Venook, MD	4	3	2	1	4	3	2	1	
Moderator	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 moderator and faculty for this activity:

REQUEST FOR CREDIT — Please print clearly								
Name: Specialty:								
Degree:								
Medical License/ME Number: Last 4 Digits of SSN (required):								
Street Address: Box/Suite:								
City, State, Zip:								
Telephone: Fax:								
Email:								
Research To Practice designates this educational activity for a maximum of 2.75 AMA PRA Category 1 Credits $^{\text{TM}}$. Physicians should only claim credit commensurate with the extent of their participation in the activity.								
I certify my actual time spent to complete this educational activity to be hour(s).								
Signature: Date:								

To obtain a certificate of completion and receive credit for this activity, please complete the Post-test, fill out the Educational Assessment and Credit Form and fax both to (800) 447-4310, or mail both to Research To Practice, One Biscayne Tower, 2 South Biscayne Boulevard, Suite 3600, Miami, FL 33131. You may also complete the Post-test and Educational Assessment online at www.ResearchToPractice.com/CCU/ThinkTank/CME.

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

Colorectal Cancer™

Moderator Managing Editor Neil Love, MD Kathryn Ault Ziel, PhD

Scientific Director

Richard Kaderman, PhD

Senior Director, Medical Affairs

Aviva Asnis-Alibozek, PA-C, MPAS Lilliam Sklaver Poltorack, PharmD

Writers

Douglas Paley

Continuing Education Administrator for Nursing Content Validation Sally Bogert, RNC, WHCNP

Margaret Peng

Erin Wall

Clayton Campbell Jessica McCarrick

Director, Creative and Copy Editing

Aura Herrmann

Creative Manager Graphic Designers Fernando Rendina Jessica Benitez

Jason Cunnius Tamara Dabney

Shantia Daniel Claudia Munoz

Senior Production Editor Traffic Manager Alexis Oneca Tere Sosa

Copy Editors Dave Amber
Margo Harris
David Hill
Rosemary Hul

Rosemary Hulce Kirsten Miller Pat Morrissey/Havlin Carol Peschke

Susan Petrone Tracy Potter

Production Manager Audio Production

Production Frank Cesarano
Web Master John Ribeiro

Faculty Relations Manager CME Director/CPD Director

Contact Information

Melissa Vives Isabelle Tate Neil Love, MD

Research To Practice One Biscayne Tower

2 South Biscayne Boulevard, Suite 3600

Miami, FL 33131 Fax: (305) 377-9998

Email: DrNeilLove@ResearchToPractice.com

For CME/CNE Information Email: CE@ResearchToPractice.com

Copyright © 2008 Research To Practice. All rights reserved.

The compact discs, Internet content and accompanying printed material are protected by copyright. No part of this program may be reproduced or transmitted in any form or by any means, electronic or mechanical, including photocopying, recording or utilizing any information storage and retrieval system, without written permission from the copyright owner.

The opinions expressed are those of the presenters and are not to be construed as those of the publisher or grantors.

Participants have an implied responsibility to use the newly acquired information to enhance patient outcomes and their

own professional development. The information presented in this activity is not meant to serve as a guideline for patient management.

Any procedures, medications or other courses of diagnosis or treatment discussed or suggested in this activity should not be used by clinicians without evaluation of their patients' conditions and possible contraindications or dangers in use, review of any applicable manufacturer's product information and comparison with recommendations of other authorities.

Colorectal Cancer

Copyright © 2008 Research To Practice.

This program is supported by educational grants from
AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company,
Genentech BioOncology, Genomic Health Inc and ImClone Systems Incorporated.

Research To Practice®

Sponsored by Research To Practice.

Last review date: December 2008 Release date: December 2008 Expiration date: December 2009 Estimated time to complete: 2.75 hours





