

Colorectal Cancer™

U P D A T E

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

EDITOR

Neil Love, MD

ROUNDTABLE DISCUSSION

Axel Grothey, MD

Neal J Meropol, MD

Alan P Venook, MD

INTERVIEWS

David A Geller, MD

Eric Van Cutsem, MD, PhD

Robert J Mayer, MD



Colorectal Cancer Update

A Continuing Medical Education Audio Series

STATEMENT OF NEED/TARGET AUDIENCE

Colorectal cancer is among the most common types of cancer in the United States, and the arena of colorectal cancer treatment continues to evolve. Published results from ongoing clinical trials lead to the emergence of new therapeutic agents and regimens and changes in the indications, doses and schedules for existing treatments. 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* utilizes one-on-one discussions with leading oncology investigators. By providing access to the latest research developments and expert perspectives, this CME activity assists medical oncologists with the formulation of up-to-date clinical management strategies.

LEARNING OBJECTIVES

- Evaluate the role of K-ras mutations in the selection of patients with colorectal cancer (CRC) for treatment with EGFR inhibitors.
- Develop an evidence-based algorithm for the treatment of metastatic CRC that incorporates bevacizumab, cetuximab and other biologic agents, based on an understanding of the efficacy and tolerability of these regimens.
- Develop an evidence-based algorithm for the adjuvant treatment of localized Stage II and Stage III colon cancer, based on an understanding of the benefits and risks of adjuvant systemic therapy.
- Summarize clinical factors that influence decisions about resectability of hepatic CRC metastases in order to facilitate identification of patients who may benefit from surgery.
- Evaluate the role of perioperative chemotherapy and surgery versus surgery alone to assist in treatment planning for patients with resectable hepatic CRC metastases.
- Counsel appropriately selected patients about the availability of ongoing clinical trials in which they may be eligible to participate.

PURPOSE OF THIS ISSUE OF *COLORECTAL CANCER UPDATE*

The purpose of Issue 2 of *Colorectal Cancer Update* is to support the learning objectives by offering the perspectives of Drs Geller, Grothey, Mayer, Meropol, Van Cutsem and Venook on the integration of emerging clinical research data into the management of colorectal cancer.

ACCREDITATION STATEMENT

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**3 TUMOR PANEL DISCUSSION:
PERSONAL CASES FROM THE FACULTY**

Axel Grothey, MD

Professor of Oncology
Department of Medical Oncology
Mayo Clinic
Rochester, Minnesota

Neal J Meropol, MD

Director, Gastrointestinal Cancer Program
Director, Gastrointestinal Tumor Risk Assessment Program
Divisions of Medical Science and Population Science
Fox Chase Cancer Center
Philadelphia, Pennsylvania

Alan P Venook, MD

Professor of Clinical Medicine
University of California, San Francisco
San Francisco, California

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David A Geller, MD

Richard L Simmons Professor of Surgery
Co-Director, UPMC Liver Cancer Center
University of Pittsburgh
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Pittsburgh, Pennsylvania

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University Hospital Gasthuisberg
Leuven, Belgium

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Director, Center for Gastrointestinal Oncology
Department of Medical Oncology
Dana-Farber Cancer Institute
Stephen B Kay Family Professor of Medicine
Harvard Medical School
Boston, Massachusetts

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FACULTY — **Prof Van Cutsem** had no real or apparent conflicts of interest to disclose. 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 Geller** — Consulting Fees: Bayer Pharmaceuticals Corporation, Onyx Pharmaceuticals Inc; Ownership Interest: Boston Scientific Corporation. **Dr Grothey** — Consulting Fees: Amgen Inc, Bristol-Myers Squibb Company, Genentech BioOncology, Roche Laboratories Inc, Sanofi-Aventis. **Dr Mayer** — Advisory Committee: Celgene Corporation; Data Safety Monitoring Committees for Two Clinical Trials: Amgen Inc. **Dr Meropol** — Consulting Fees: Amgen Inc, AstraZeneca Pharmaceuticals LP, Bristol-Myers Squibb Company, Genentech BioOncology, Genomic Health Inc, ImClone Systems Incorporated, Sanofi-Aventis. **Dr Venook** — Contracted Research: Genentech BioOncology.

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Select Excerpts from the Discussion

Case 1 from the practice of Neal J Meropol, MD

A 42-year-old woman who had been treated with adjuvant FOLFOX two years ago and now presents with multiple asymptomatic, unresectable liver metastases.

Tracks 1, 4-5, 8

► **DR LOVE:** What treatment options would you consider for this patient, outside of a clinical trial?

► **DR MEROPOL:** The first treatment option would be FOLFOX in combination with bevacizumab — considering she did not experience a tremendous amount of toxicity from FOLFOX, and she had a two-year disease-free interval. Another treatment option would be the combination of irinotecan, 5-FU and bevacizumab.

I would consider those to be the two standard treatment options. She had not received irinotecan or an antibody against the epidermal growth factor receptor (EGFR).

Those were the drugs on the table, but in taking a sequential approach, I thought it made the most sense to offer chemotherapy in combination with bevacizumab.

► **DR LOVE:** Alan, it sounds as though this patient might be eligible for your study, CALGB-C80405, evaluating the combination of chemotherapy and biologic agents as front-line therapy for metastatic colorectal cancer. Can you describe the design of that trial?

► **DR VENOOK:** In this trial, the choice of chemotherapy regimen — FOLFOX or FOLFIRI — is left up to the physician and the patient to decide. Then patients are randomly assigned to cetuximab alone, cetuximab with bevacizumab or bevacizumab alone (1.1). Indeed, a patient such as this one — who completed adjuvant FOLFOX more than a year earlier — would be eligible for enrollment.

► **DR LOVE:** Axel, in terms of the issue of combining bevacizumab with an anti-EGFR antibody, what exactly do we know about the PACCE trial and panitumumab?

► **DR GROTHEY:** The PACCE trial had two cohorts — one cohort received an oxaliplatin-based regimen, and the other cohort received an irinotecan-based regimen. The data from the cohort that received irinotecan-based chemotherapy were reported. Approximately 200 patients were randomly assigned to irinotecan/5-FU/bevacizumab with or without panitumumab as first-line therapy.

The data revealed the activity of panitumumab — an antibody that targets EGFR — in patients with tumors that had wild-type versus mutant K-ras. Patients whose tumors had mutant K-ras received no benefit — in terms of response rate — from panitumumab in combination with irinotecan/5-FU/bevacizumab.

In contrast, patients whose tumors had wild-type K-ras had a higher response rate when panitumumab was combined with irinotecan/5-FU/bevacizumab (Hecht 2008; [1.2]).

- ▶ **DR LOVE:** What proportion of patients have a tumor with a K-ras mutation?
- ▶ **DR GROTHEY:** Approximately 40 to 45 percent have a K-ras mutation. One caveat is that those patients have a poorer prognosis.

1.1

Phase III Randomized Study of Cetuximab and/or Bevacizumab in Combination with Either FOLFOX or FOLFIRI

Protocol IDs: CALGB-C80405, C80405, SWOG-C80405, NCT00265850
 Target Accrual: 2,300 (Open)



Patients are stratified according to physician-selected chemotherapy (FOLFOX versus FOLFIRI), prior adjuvant chemotherapy (yes versus no) and prior pelvic radiation therapy (yes versus no).

In all arms, treatment repeats every 56 days for at least two courses in the absence of disease progression, unacceptable toxicity or planned surgery with curative intent.

For patients for whom elective surgery is contemplated, bevacizumab must be discontinued for at least eight weeks before surgery and may not be resumed for at least four weeks after surgery. Patients who undergo complete resection of metastatic disease are removed from the study.

Study Contacts

Cancer and Leukemia Group B
 Alan P Venook, MD
 Tel: 415-353-7065, 800-888-8664

Southwest Oncology Group
 Charles Blanke, MD, FACP
 Tel: 503-494-1556, 800-494-1234

SOURCE: NCI Physician Data Query, April 2008.

1.2

PACCE Trial: Interim Results Evaluating Irinotecan-Based Chemotherapy and Bevacizumab (IRI-CT/BEV) with or without Panitumumab as First-Line Therapy for Metastatic Colorectal Cancer

Overall response rate according to K-ras status
 (Central review)

Mutant K-ras		Wild-type K-ras	
Panitumumab + IRI-CT/BEV (n = 46)	IRI-CT/BEV alone (n = 39)	Panitumumab + IRI-CT/BEV (n = 57)	IRI-CT/BEV alone (n = 58)
30%	38% ¹	54%	47% ²

¹ Odds ratio = 0.59 (95% CI: 0.23-1.55); ² odds ratio = 1.42 (95% CI: 0.63-3.21); odds ratio for panitumumab:control (>1 favors panitumumab + IRI-CT/BEV)

SOURCE: Hecht JR et al. Gastrointestinal Cancers Symposium 2008; [Abstract 279](#).



Tracks 11, 13, 15

Case 2 from the practice of Alan P Venook, MD

A healthy 80-year-old woman underwent a right hemicolectomy for nearly obstructing colon cancer and was found to have zero out of 11 involved lymph nodes.

► **DR LOVE:** Alan, does this woman have high-risk Stage II disease?

► **DR VENOOK:** Her high-risk feature was the 11 lymph nodes examined. She had radiographic evidence of a near obstruction, but she was asymptomatic. After a long discussion with the patient and her family, we decided not to use adjuvant therapy.

► **DR MEROPOL:** The fact that she had no symptoms is important in assessing her risk. The studies that examined obstruction as an indicator of poor prognosis or a high-risk feature were conducted in patients who presented with frank bowel obstruction or clear radiographic evidence of a bowel obstruction that required emergency surgery.

► **DR LOVE:** What about the number of nodes examined? Interestingly, the Adjuvant! Online model uses a cutoff of 10 nodes.

► **DR MEROPOL:** A number of studies suggest that the number of lymph nodes evaluated is probably a continuous variable. For quality assurance purposes, the notion was accepted that the evaluation of 12 lymph nodes was a good cutoff and the number we should aspire to and that patients with fewer than 12 nodes examined ought to be considered at high risk, at least in some way.

I have two comments regarding this issue. First, in general, it's not dichotomous — fewer than 12, more than 12. Indeed, 11 lymph nodes is pretty close to 12, and it is not the same situation as a patient who has zero nodes evaluated. Second, a contrarian view was raised in a paper published in the *Journal of the American Medical Association* using a large administrative data set, which suggested that in Stage II colon cancer, the number of lymph nodes examined does not imply risk (Wong 2007).

► **DR LOVE:** Neal, this woman is 80 years old. How would each of you treat an otherwise healthy, 55-year-old patient who has Stage II disease without any high-risk factors?

► **DR MEROPOL:** For me, it's probably a 50/50 split between treating with a fluoropyrimidine — usually capecitabine — or nothing.

► **DR VENOOK:** I agree. I would use capecitabine alone or nothing at all, depending on other issues.

► **DR GROTHEY:** I find it useful to sit down with patients, view their case on Adjuvant! Online and print out the data. I would not exclude oxaliplatin-based therapy for these patients.

Case 3 from the practice of Axel Grothey, MD

A 76-year-old man who presents with nearly obstructing colorectal cancer, multiple hepatic metastases and a poor performance status.

► **DR LOVE:** How did you approach this patient, Axel?

► **DR GROTHEY:** My first discussion with the patient included asking what he wanted to accomplish with therapy. He was recently widowed, was depressed and lived alone.

At first he said, “I don’t know whether it’s worth it.” Then he asked, “So, what are we talking about here?” I explained that considering how his tumor was progressing and his physical condition, if we did not use antitumor therapy, he might survive only a matter of weeks, but I believed if the tumor responded well to therapy, being alive in a year was achievable and I would consider that a success.

He decided he wanted therapy, and we started with FOLFOX. I did not administer bevacizumab during the first cycle. I didn’t even implant a Port-A-Cath® because I wasn’t certain we’d complete the first cycle of FOLFOX. I saw him weekly because I wanted to make sure he didn’t develop any problems, and I omitted the bolus 5-FU to reduce the risk of complications.

The bleeding stopped almost immediately, his bilirubin dropped significantly and he felt better. I added bevacizumab from the second cycle on. After four cycles of therapy, his liver was no longer palpable. Initially, his CEA level was in the range of 500 ng/mL, and it normalized with therapy, as did his LDH level. It was one of the most dramatic responses I have ever seen.

Although he benefited from therapy, it didn’t last long. He had problems with toxicities in the end. In spite of omitting the bolus 5-FU, he had some neutropenia and infectious complications. His tumor was controlled as long as we continued therapy, but about nine months later he said, “I think this is it. We’ve done exactly what we wanted to do, and you’ve given me some time.” So we stopped therapy, and he died almost exactly one year after he started therapy. ■

SELECT PUBLICATIONS

Amado RG et al. **Panitumumab (pmab) efficacy and patient-reported outcomes (PRO) in metastatic colorectal cancer (mCRC) patients (pts) with wild-type (WT) KRAS tumor status.** Gastrointestinal Cancers Symposium 2008; [Abstract 278](#).

Hecht JR et al. **Interim results from PACCE: Irinotecan (Iri)/bevacizumab (bev) ± panitumumab (pmab) as first-line treatment (tx) for metastatic colorectal cancer (mCRC).** Gastrointestinal Cancers Symposium 2008; [Abstract 279](#).

Wong SL et al. **Hospital lymph node examination rates and survival after resection for colon cancer.** *JAMA* 2007;298(18):2149-54. [Abstract](#)



INTERVIEW

David A Geller, MD

Dr Geller is Richard L Simmons Professor of Surgery and Co-Director of the UPMC Liver Cancer Center at the University of Pittsburgh Starzl Transplant Institute in Pittsburgh, Pennsylvania.

Tracks 1-8

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| Track 2 | Specialty surgical training and outcomes from resection of liver metastases | Track 6 | Influence of the number of hepatic metastases on resectability |
| Track 3 | Therapeutic approach for patients with a synchronous primary tumor and liver metastases | Track 7 | Novel treatment approaches for liver metastases |
| Track 4 | Diminished or absent role of hepatic arterial infusion in an era of newer-generation systemic therapies | Track 8 | Surgeon's perspective on the efficacy and tolerability of newer chemotherapy regimens in CRC |

Select Excerpts from the Interview

Track 3

► **DR LOVE:** What is your usual treatment approach for patients who present with a simultaneous primary colon cancer and resectable liver metastases?

► **DR GELLER:** If the patient is a reasonably healthy 40- or 50-year-old, I'll work with the chief of colorectal surgery and we'll perform a simultaneous colon resection — such as a lower anterior resection or right hemicolectomy — in addition to a liver resection.

This approach requires two perfect operations — a perfect colon resection and a technically perfect liver resection — because a complication in one can hinder the outcome of the other. We have probably performed 20 such operations in the last three years at Pittsburgh, and the outcomes have been excellent.

That's not what generally happens in the community. It's perfectly fine for the colorectal surgeon or the general surgeon to perform the colectomy. Most of those patients will have positive lymph nodes. If the surgeon can see the liver lesion at the time of the colon resection, I recommend a needle biopsy for

confirmation. It just takes an extra moment, and then we don't have to subject the patient to a biopsy later.

I'm never in a rush to operate on the liver. We let the patients recover from the colon surgery, complete their staging and administer two or three cycles of adjuvant chemotherapy. At three months, we restage with a CT/PET scan. If they have stable disease or a slight improvement, that's the perfect time to perform the liver resection.

We don't want the patients to receive six or nine months of chemotherapy because it damages the liver and causes steatosis or, worse, steatohepatitis. A syndrome called chemotherapy-associated steatohepatitis (CASH) is similar to nonalcoholic steatohepatitis (NASH) — fatty liver disease. Chemotherapy can cause the same condition, and fatty livers do not tolerate major hepatic resections.

Track 4

▶ **DR LOVE:** Is there a current role for intrahepatic infusion of chemotherapy?

▶ **DR GELLER:** Intrahepatic infusion of chemotherapy has fallen by the wayside. In December 1999, Kemeny's article appeared in *The New England Journal of Medicine* and repopularized the placement of hepatic artery pumps for infusional therapy (Kemeny 1999). The only drug approved in the US was floxuridine — a cousin of 5-FU.

However, that was in an era in which we didn't have these three- and four-drug combinations, whereas now, we are seeing the response rates around 50 percent. We can avoid the morbidities associated with the pumps, including a 20 percent incidence of biliary sclerosis from infusional floxuridine that is often irreversible.

I don't believe much of a role exists for a pump in a patient who has received FOLFOX or FOLFIRI, and we see almost no referrals. In the last three years with the newer drug combinations, I've placed maybe two pumps and those were for patients who had failed systemic chemotherapy.

I believe the only role for hepatic artery pumps is in a randomized trial in which systemic chemotherapy is combined with intrahepatic infusional chemotherapy.

Track 5

▶ **DR LOVE:** What are the surgical considerations in hepatic resection for a patient who receives bevacizumab?

▶ **DR GELLER:** Bevacizumab can hinder wound healing, and it's associated with an increased incidence of bleeding and cardiac events. Patients can even develop thrombotic events. Therefore, we need to use this agent cautiously in patients with a poor cardiac history.

In cases in which the patient is to receive FOLFOX combined with bevacizumab, I work with the oncologist to come up with a plan. Typically, patients will receive a couple of cycles of chemotherapy with bevacizumab, and then both the oncologist and I will see them. If the plan is to perform a liver resection, we'll administer a third cycle of chemotherapy without bevacizumab.

I prefer for patients to be off of chemotherapy for three weeks before surgery — so the immune system recovers from the bone marrow nadir — and off of bevacizumab for six weeks. We've seen no complications when we have a four- to six-week window without bevacizumab.

Track 6

► **DR LOVE:** Is there a specific number of liver metastases that you would not be willing to resect?

► **DR GELLER:** If you look beyond a decade ago, the classic belief was that patients with up to four tumors in the liver were candidates for resection. Today, we resect way beyond that number — we push the envelope and resect as many as five to eight tumors. If I can remove all of the cancer safely and preserve enough liver mass, then that is the preferred approach.

In patients with only one metastatic lesion, resection alone will cure them approximately 40 percent of the time. However, that means 60 percent will experience recurrence. We have a few prognostic indicators, but we don't yet have good biomarkers to predict which patients will experience a recurrence. In addition, if a patient has six or seven hepatic metastases, the chance for recurrence is much greater than for someone who has a solitary lesion. Therefore, I recommend that all patients receive some adjuvant chemotherapy after resection. ■

SELECT PUBLICATIONS

Fong Y, Bentrem DJ. **CASH (Chemotherapy-Associated Steatohepatitis) costs.** *Ann Surg* 2006;243(1):8-9. No abstract available

Kandutsch S et al. **Patterns of hepatotoxicity after chemotherapy for colorectal cancer liver metastases.** *Eur J Surg Oncol* 2008;[Epub ahead of print]. [Abstract](#)

Kemeny N et al. **Hepatic arterial infusion of chemotherapy after resection of hepatic metastases from colorectal cancer.** *N Engl J Med* 1999;341(27):2039-48. [Abstract](#)

Morris-Stiff G et al. **Hepatic complications following preoperative chemotherapy with oxaliplatin or irinotecan for hepatic colorectal metastases.** *Eur J Surg Oncol* 2007;[Epub ahead of print]. [Abstract](#)

Pasetto LM et al. **Hepatic metastases of colorectal cancer: Locoregional intra-arterial treatment.** *Anticancer Res* 2006;26(6C):4785-92. [Abstract](#)

Pawlik TM, Choti MA. **Surgical therapy for colorectal metastases to the liver.** *J Gastrointest Surg* 2007;11(8):1057-77. [Abstract](#)

Wei AC et al. **Survival after hepatic resection for colorectal metastases: A 10-year experience.** *Ann Surg Oncol* 2006;13(5):668-76. [Abstract](#)

Zorzi D et al. **Chemotherapy-associated hepatotoxicity and surgery for colorectal liver metastases.** *Br J Surg* 2007;94(3):274-86. [Abstract](#)



INTERVIEW

Eric Van Cutsem, MD, PhD

Prof Van Cutsem is Professor of Medicine at University Hospital Gasthuisberg in Leuven, Belgium.

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- Track 1** Preoperative evaluation of patients with liver-only metastases
- Track 2** EORTC-40983: Perioperative FOLFOX4 and surgery versus surgery alone for resectable liver metastases from CRC
- Track 3** Clinical use of preoperative chemotherapy for patients with resectable liver metastases
- Track 4** Pre- and postoperative versus postoperative-only chemotherapy for patients with resectable liver metastases
- Track 5** Integrating biologic agents into neoadjuvant or adjuvant therapy
- Track 6** Imaging studies for patients treated with biologic agents
- Track 7** K-ras mutation status and benefit from EGFR inhibitors
- Track 8** Revised eligibility criteria for trials evaluating EGFR inhibitors
- Track 9** Relative efficacy of panitumumab and cetuximab
- Track 10** Efficacy of bevacizumab in combination with FOLFOX as first-line therapy
- Track 11** Continuation of bevacizumab upon disease progression
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- Track 13** Adjuvant trials of bevacizumab
- Track 14** Neoadjuvant bevacizumab for patients with initially unresectable liver metastases
- Track 15** Clinical use of FOLFOX/cetuximab/bevacizumab
- Track 16** PACCE: Chemotherapy/bevacizumab with or without panitumumab as first-line therapy for mCRC
- Track 17** Potential adjuvant trial of FOLFOX in combination with bevacizumab and cetuximab
- Track 18** Neoadjuvant trial of bevacizumab in rectal cancer

Select Excerpts from the Interview

Tracks 2, 4

► **DR LOVE:** Can you discuss the results from the EORTC-40983 trial?

► **PROF VAN CUTSEM:** In the EORTC-40983 study, patients with resectable liver metastases received six cycles of FOLFOX4 before and after resection (perioperative chemotherapy). The progression-free survival for the patients treated with perioperative chemotherapy was better than that for patients who

underwent surgery alone. We also saw slightly more postoperative complications among the patients who received perioperative chemotherapy than among those who underwent surgery alone. Although slightly more morbidity was observed, the postoperative mortality was identical (Nordlinger 2008; [2.1]).

The three-month duration of preoperative treatment is important. In other studies, when patients received more than three months of treatment, the complication rate increased. Patients with initially unresectable metastases should undergo surgery as soon as their disease becomes resectable. If the patient's disease becomes resectable, chemotherapy should not continue until a maximum response is observed.

One reason for this is the increased risk of complications. The other reason is that if you continue to treat, the metastases may cease to appear on a CT scan, which can be a nightmare for the surgeons. Perhaps that's an overstatement, but it's extremely difficult for them to find the lesions if they don't see the correlation on imaging. Upon resection, more than 80 percent of the areas in which there was initially a metastasis but then nothing is seen on a CT scan will still have microscopic lesions.

► **DR LOVE:** Could we have achieved the same results with postoperative therapy alone?

► **PROF VAN CUTSEM:** Formally, we do not have proof that perioperative followed by postoperative therapy is better than only postoperative therapy. However, for rectal cancer and many other types of cancer, preoperative treatment has several advantages: It's better tolerated, and there are oncologic advantages. At ASCO last year, Nick Petrelli suggested a randomized trial to evaluate these two options. I believe it would be extremely difficult to conduct such a trial, and more important questions must be addressed to make progress in these patients.

Tracks 10-11

► **DR LOVE:** Where are we now in terms of clinical research on bevacizumab?

► **PROF VAN CUTSEM:** We have seen in the past year — in a formal randomized trial in the first-line setting — that bevacizumab increases the activity of oxaliplatin-based regimens (Saltz 2008). We already knew from ECOG-E3200, the second-line study of FOLFOX with or without bevacizumab, that the addition of bevacizumab was positive (Giantonio 2007). We also knew that bevacizumab increased the activity of 5-FU (Hurwitz 2005) and irinotecan/5-FU (Hurwitz 2004) as first-line therapy. So the picture is becoming more complete, and more formal evidence is accumulating.

An issue we don't have a formal answer to is the continuation of bevacizumab after disease progression. Data from the BRiTE registry — presented last year at ASCO — suggested that for patients whose disease is progressing on chemotherapy and bevacizumab, switching the chemotherapy but continuing bevacizumab produces a better outcome (Grothey 2007; [2.2]).

It's not a randomized trial, but the BRiTE data and some preclinical data suggest that continuation of bevacizumab might benefit at least a subgroup of patients. We need the formal comparison conducted in this setting.

- ▶ **DR LOVE:** Is that what's going to happen in the iBET study?
- ▶ **PROF VAN CUTSEM:** Yes. iBET is presently recruiting (2.3). However, I understand from my American colleagues that accrual is not progressing quickly. A German group is conducting a similar but more flexible study in that patients can be treated with any irinotecan- or oxaliplatin-based regimen with bevacizumab as first-line therapy, and then they change to another chemotherapy regimen with or without bevacizumab in the second-line setting. ■

2.1 Trial Evaluating the Benefit of Perioperative FOLFOX4 for Patients with Potentially Resectable CRC Hepatic Metastases

Protocol ID: EORTC-40983; Accrual: 364 (Closed)



	Perioperative FOLFOX4 + surgery	Surgery alone	HR (95.66% CI)	p-value
Three-year progression-free survival				
All patients randomly assigned (n = 182, 182)	35.4%	28.1%	0.79 (0.62-1.02)	0.058
All patients who underwent resection (n = 152, 151)	42.4%	33.2%	0.73 (0.55-0.97)	0.025
Reversible postoperative complications (n = 159, 170)	25%	16%	—	0.04
Postoperative death (n = 159, 170)	1%	1%	—	—

HR = hazard ratio; CI = confidence interval

SOURCE: Nordlinger B et al. *Lancet* 2008;371(9617):1007-16. [Abstract](#)

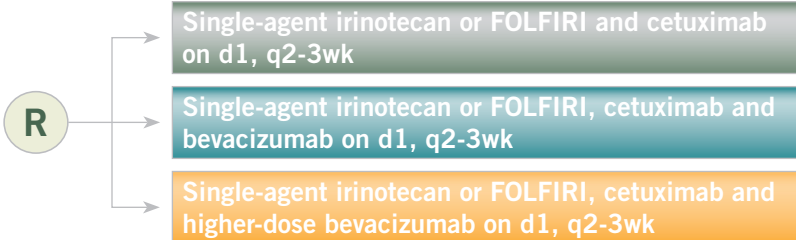
2.2 BRiTE: Survival with and without Bevacizumab Beyond Progression

Outcomes	Bevacizumab beyond progression (n = 642)	No bevacizumab beyond progression (n = 531)
Overall survival	31.8mo	19.9mo
One-year survival	87.7%	77.3%
Survival beyond first progressive disease	19.2mo	9.5mo

SOURCE: Grothey A et al. *Proc ASCO* 2007; [Abstract 4036](#).

iBET: A Phase III Study of Irinotecan-Based Therapy and Cetuximab with or without Bevacizumab in Metastatic Colon Cancer After Disease Progression on Bevacizumab-Containing First-Line Therapy

Protocol IDs: SWOG-S0600, NCT00499369
Target accrual: 1,260 (Open)



Eligibility

- Confirmed metastatic disease with disease progression after first-line therapy with bevacizumab and FOLFOX, OPTIMOX or XELOX
- No prior irinotecan or cetuximab
- Zubrod PS 0 to 2
- No uncontrolled hypertension (ie, SBP > 150 mmHg or DBP > 90 mmHg)

SOURCE: NCI Physician Data Query, April 2008.

SELECT PUBLICATIONS

Benoist S et al. **Complete response of colorectal liver metastases after chemotherapy: Does it mean cure?** *J Clin Oncol* 2006;24(24):3939-45. [Abstract](#)

Giantonio BJ et al. **Bevacizumab in combination with oxaliplatin, fluorouracil, and leucovorin (FOLFOX4) for previously treated metastatic colorectal cancer: Results from the Eastern Cooperative Oncology Group Study E3200.** *J Clin Oncol* 2007;25(12):1539-44. [Abstract](#)

Grothey A et al. **Association between exposure to bevacizumab (BV) beyond first progression (BBP) and overall survival (OS) in patients (pts) with metastatic colorectal cancer (mCRC): Results from a large observational study (BRiTE).** *Proc ASCO* 2007;[Abstract 4036](#).

Hurwitz HI et al. **Bevacizumab in combination with fluorouracil and leucovorin: An active regimen for first-line metastatic colorectal cancer.** *J Clin Oncol* 2005;23(15):3502-8. [Abstract](#)

Hurwitz H et al. **Bevacizumab plus irinotecan, fluorouracil, and leucovorin for metastatic colorectal cancer.** *N Engl J Med* 2004;350(23):2335-42. [Abstract](#)

Nordlinger B et al. **Perioperative chemotherapy with FOLFOX4 and surgery versus surgery alone for resectable liver metastases from colorectal cancer (EORTC Intergroup trial 40983): A randomised controlled trial.** *Lancet* 2008;371(9617):1007-16. [Abstract](#)

Saltz LB et al. **Bevacizumab in combination with oxaliplatin-based chemotherapy as first-line therapy in metastatic colorectal cancer: A randomized phase III study.** *J Clin Oncol* 2008;26(12):2013-9. [Abstract](#)

Van Cutsem E et al. **Randomized phase III study of irinotecan and 5-FU/FA with or without cetuximab in the first-line treatment of patients with metastatic colorectal cancer (mCRC): The CRYSTAL trial.** *Proc ASCO* 2007;[Abstract 4000](#).



INTERVIEW

Robert J Mayer, MD

Dr Mayer is Director of the Center for Gastrointestinal Oncology in the Department of Medical Oncology at the Dana-Farber Cancer Institute and is Stephen B Kay Family Professor of Medicine at Harvard Medical School in Boston, Massachusetts.

Tracks 1-13

- | | | | |
|----------------|---|-----------------|---|
| Track 1 | Recent advances and future directions in the management of CRC | Track 7 | Observation or delayed initiation of palliative therapy for patients with mCRC |
| Track 2 | CALGB-C89803: Microsatellite instability predicts benefit from adjuvant irinotecan | Track 8 | Combination versus sequential therapy for patients with mCRC |
| Track 3 | Influence of diet and exercise on colon cancer recurrence | Track 9 | Duration of watchful waiting for patients with mCRC |
| Track 4 | K-ras mutations and efficacy of EGFR inhibitors | Track 10 | Use of “drug holidays” in the management of mCRC |
| Track 5 | Gene assays to predict benefit from adjuvant therapy | Track 11 | Transitioning to hospice care |
| Track 6 | PACCE: First-line therapy with chemotherapy/bevacizumab with or without panitumumab in mCRC | Track 12 | Clinical use of CT scans in the follow-up of patients with CRC |
| | | Track 13 | Clinical use of neoadjuvant therapy for patients with resectable liver metastases |

Select Excerpts from the Interview

Track 3

► **DR LOVE:** Can you discuss the analysis of CALGB-C89803 with regard to the influence of diet and exercise on colon cancer recurrence?

► **DR MAYER:** Jeff Meyerhardt and Charlie Fuchs, based on their experience with the Nurses’ Health Study, developed a prospective questionnaire about the effects of diet, exercise and lifestyle on colon cancer recurrence. We have also collected blood samples, and we’ll be able to determine prospectively if different factors, such as cytokines and insulin growth factor receptors, correlate.

They found that a Western diet that includes lots of fats and obesity may be associated with a higher risk of recurrence and mortality (Meyerhardt 2007; [3.1]). Perhaps, as you become obese or develop type II diabetes, you also stimulate a variety of hormone cytokines — factors that may activate microscopic tumor cells. A strong association between exercise and reduced risk of cancer relapse was also seen (Meyerhardt 2006).

3.1

Associations between Colon Cancer Recurrence and Mortality and the Western Dietary Pattern¹

Parameter	Western dietary pattern by quintile ²					<i>p</i> for trend
	1 (n = 201)	2 (n = 202)	3 (n = 202)	4 (n = 202)	5 (n = 202)	
Disease-free survival ³	Reference	0.98	1.51	1.64	3.25	<0.001
Recurrence-free survival ³	Reference	0.92	1.42	1.44	2.85	<0.001
Overall mortality ³	Reference	0.74	1.38	1.66	2.32	<0.001

¹ Median follow-up of patients was 5.3 years from completion of the first questionnaire and 5.6 years from trial entry.

² Higher quintiles are indicative of higher intake of the Western dietary pattern.

³ Adjusted for sex, age, depth of invasion through bowel wall (T1-2 versus T3-4), number of positive lymph nodes (1-3 versus ≥ 4), presence of clinical perforation at time of surgery, presence of bowel obstruction at time of surgery, baseline performance status (0 versus 1-2), treatment group, weight change between first and second questionnaire, time-varying body mass index, time-varying physical activity level and time-varying total calories

SOURCE: Meyerhardt JA et al. *JAMA* 2007;298(7):754-64. [Abstract](#)

Track 4

► **DR LOVE:** What are your thoughts on evolving data evaluating K-ras and the EGFR inhibitors?

► **DR MAYER:** A paper recently published in the *Journal of Clinical Oncology* had fascinating, clearly stated data on the correlation of K-ras mutations and lack of response to cetuximab (Lièvre 2008). At the ASCO GI 2008 meeting, Amado and colleagues presented panitumumab data from Europe broken down by K-ras mutation status (Amado 2008; [3.2]). These data explain to an enormous degree why the combination regimen in the large Phase III SWOG-S0205 trial evaluating gemcitabine/cetuximab versus gemcitabine alone in patients with pancreatic cancer showed no benefit (Phillip 2007), because essentially 98 to 99 percent of pancreatic cancer cases have K-ras mutations — those tumors do not respond to treatment. In colon cancer, approximately 40 percent of patients have the K-ras mutation.

Track 6

► **DR LOVE:** Where do you think we might be headed in terms of the concept of double antibody therapy for advanced colorectal cancer?

► **DR MAYER:** That's a controversial issue because of the results of the PACCE study presented at the 2008 ASCO GI meeting (Hecht 2008a, 2008b). The PACCE study is a randomized trial in which four out of five patients receive

FOLFOX — the remaining patients receive FOLFIRI — and are then randomly assigned to receive bevacizumab alone or with panitumumab. To everyone’s surprise, PACCE has shown seeming detriment and increased toxicity.

Some people argue that bevacizumab works as an anti-angiogenesis drug. However, others would argue that bevacizumab works by increasing the permeability of the cell membranes, thereby modulating chemotherapy and increasing chemotherapy concentrations within the cell. Could that be interfering with the binding of a compound such as cetuximab or panitumumab to the cell surface? We do not have answers at the moment, and the analysis isn’t yet in on the PACCE study. ■

3.2

Panitumumab and Best Supportive Care (BSC) versus BSC Alone in Patients with Chemotherapy-Refractory Metastatic Colorectal Cancer: Efficacy According to K-ras Status

	Mutant K-ras		Wild-type K-ras	
	Panitumumab + BSC (n = 84)	BSC alone (n = 100)	Panitumumab + BSC (n = 124)	BSC alone (n = 119)
Median progression-free survival	7.4 weeks	7.3 ¹ weeks	12.3 weeks	7.3 ² weeks
Median overall survival	4.9 months	4.4 months	8.1 months	7.6 months

¹ Hazard ratio = 0.99 (95% CI: 0.73-1.36); ² hazard ratio = 0.45 (95% CI: 0.34-0.59) *p* < 0.0001

SOURCE: Amado RG et al. Gastrointestinal Cancers Symposium 2008; [Abstract 278](#).

SELECT PUBLICATIONS

Amado RG et al. **Panitumumab (pmab) efficacy and patient-reported outcomes (PRO) in metastatic colorectal cancer (mCRC) patients (pts) with wild-type (WT) KRAS tumor status.** Gastrointestinal Cancers Symposium 2008; [Abstract 278](#).

Hecht JR et al. **An updated analysis of safety and efficacy of oxaliplatin (Ox)/bevacizumab (bev) +/- panitumumab (pmab) for first-line treatment (tx) of metastatic colorectal cancer (mCRC) from a randomized, controlled trial (PACCE).**

Gastrointestinal Cancers Symposium 2008a; [Abstract 273](#).

Hecht JR et al. **Interim results from PACCE: Irinotecan (Iri)/bevacizumab (bev) ± panitumumab (pmab) as first-line treatment (tx) for metastatic colorectal cancer (mCRC).** Gastrointestinal Cancers Symposium 2008b; [Abstract 279](#).

Lièvre A et al. **KRAS mutations as an independent prognostic factor in patients with advanced colorectal cancer treated with cetuximab.** *J Clin Oncol* 2008;26(3):374-9.

[Abstract](#)

Meyerhardt JA et al. **Association of dietary patterns with cancer recurrence and survival in patients with Stage III colon cancer.** *JAMA* 2007;298(7):754-64. [Abstract](#)

Meyerhardt JA et al. **Impact of physical activity on cancer recurrence and survival in patients with stage III colon cancer: Findings from CALGB 89803.** *J Clin Oncol* 2006;24(22):3535-41. [Abstract](#)

Phillip PA et al. **Phase III study of gemcitabine [G] plus cetuximab [C] versus gemcitabine in patients [pts] with locally advanced or metastatic pancreatic adenocarcinoma [PC]: SWOG S0205 study.** *Proc ASCO* 2007; [Abstract LBA4509](#).

QUESTIONS (PLEASE CIRCLE ANSWER):

- In CALGB-C80405, which evaluates chemotherapy in combination with cetuximab and/or bevacizumab for previously untreated metastatic colorectal cancer, the chemotherapy regimen used is _____.
 - FOLFOX
 - FOLFIRI
 - FOLFOX or FOLFIRI, at the discretion of the physician
- In the clinical trial evaluating best supportive care with or without panitumumab for chemotherapy-refractory metastatic colorectal cancer, panitumumab improved progression-free survival for the patients with tumors that had _____ K-ras.
 - Mutant
 - Wild-type
- In EORTC-40983, perioperative chemotherapy was associated with _____ compared to surgical resection alone in patients with resectable liver metastases.
 - Improved progression-free survival
 - More postoperative complications
 - Higher postoperative mortality
 - Both a and b
- Of patients whose liver metastases disappear on imaging after preoperative chemotherapy, _____ have microscopic metastatic disease at the original lesion site.
 - 30 percent
 - 50 percent
 - 80 percent
 - 100 percent
- The Phase III randomized iBET study will evaluate the continuation of _____ after disease progression in metastatic colorectal cancer.
 - Cetuximab
 - Bevacizumab
 - Panitumumab
- In the PACCE study, _____ was found with FOLFOX/bevacizumab/panitumumab compared to FOLFOX/bevacizumab.
 - Inferior activity
 - Excess toxicity
 - Both a and b
 - None of the above
- Which dietary pattern was found to increase a patient's risk of colon cancer recurrence and mortality, as reported by Meyerhardt?
 - Western pattern (refined grains, red meats, desserts and high-fat products)
 - Prudent pattern (fruits, vegetables, whole grains, poultry and fish)
 - Either a or b
 - None of the above
- For quality assurance purposes, what is the recommended optimal number of lymph nodes that should be evaluated in a patient with resected colon cancer?
 - 24
 - 12
 - Six
 - Three
- The PACCE study is evaluating first-line therapy with chemotherapy and bevacizumab with or without _____ in patients with metastatic colorectal cancer.
 - Cetuximab
 - Gemcitabine
 - Panitumumab

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?

4 = Expert 3 = Above average 2 = Competent 1 = Insufficient

- Impact of K-ras mutations on response to EGFR inhibitors4 3 2 1
- Combining biologic agents for the treatment of advanced colorectal cancer ...4 3 2 1
- Role of perioperative chemotherapy in patients with resectable hepatic metastases ...4 3 2 1
- Continuation of biologic agents beyond disease progression4 3 2 1

AFTER completion of this activity, how would you characterize your level of knowledge on the following topics?

4 = Expert 3 = Above average 2 = Competent 1 = Insufficient

- Impact of K-ras mutations on response to EGFR inhibitors4 3 2 1
- Combining biologic agents for the treatment of advanced colorectal cancer ...4 3 2 1
- Role of perioperative chemotherapy in patients with resectable hepatic metastases ...4 3 2 1
- Continuation of biologic agents beyond disease progression4 3 2 1

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

Yes 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 expectations?

Yes No

If no, please explain:

Please respond to the following LEARNER statements 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:

- Evaluate the role of K-ras mutations in the selection of patients with colorectal cancer (CRC) for treatment with EGFR inhibitors.....4 3 2 1 N/M N/A
- Develop an evidence-based algorithm for the treatment of metastatic CRC that incorporates bevacizumab, cetuximab and other biologic agents, based on an understanding of the efficacy and tolerability of these regimens.....4 3 2 1 N/M N/A
- Develop an evidence-based algorithm for the adjuvant treatment of localized Stage II and Stage III colon cancer, based on an understanding of the benefits and risks of adjuvant systemic therapy.....4 3 2 1 N/M N/A
- Summarize clinical factors that influence decisions about resectability of hepatic CRC metastases in order to facilitate identification of patients who may benefit from surgery.....4 3 2 1 N/M N/A
- Evaluate the role of perioperative chemotherapy and surgery versus surgery alone to assist in treatment planning for patients with resectable hepatic CRC metastases.....4 3 2 1 N/M N/A
- Counsel appropriately selected patients about the availability of ongoing clinical trials in which they may be eligible to participate.....4 3 2 1 N/M N/A

What other practice changes will you make or consider making as a result of this activity?

.....

What additional information or training do you need on the activity topics or other oncology-related topics?

.....

EDUCATIONAL ASSESSMENT AND CREDIT FORM (continued)

Additional comments about this activity:

.....

.....

May we include you in future assessments to evaluate the effectiveness of this activity?

Yes No

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

Faculty	4 = Expert				3 = Above average				2 = Competent				1 = Insufficient			
	Knowledge of subject matter								Effectiveness as an educator							
David A Geller, MD	4	3	2	1	4	3	2	1	4	3	2	1	4	3	2	1
Axel Grothey, MD	4	3	2	1	4	3	2	1	4	3	2	1	4	3	2	1
Robert J Mayer, MD	4	3	2	1	4	3	2	1	4	3	2	1	4	3	2	1
Neal J Meropol, MD	4	3	2	1	4	3	2	1	4	3	2	1	4	3	2	1
Eric Van Cutsem, MD, PhD	4	3	2	1	4	3	2	1	4	3	2	1	4	3	2	1
Alan P Venook, MD	4	3	2	1	4	3	2	1	4	3	2	1	4	3	2	1

Please recommend additional faculty for future activities:

.....

Other comments about the faculty for this activity:

.....

.....

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Degree:

MD DO PharmD NP BS RN PA Other

Medical License/ME Number: Last 4 Digits of SSN (required):

Street Address: Box/Suite:

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

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