Second Opinion

Proceedings from an Interactive Case-Based Symposium on the Management of Patients with Metastatic Colorectal Cancer

CME INFORMATION

TARGET AUDIENCE

This activity is intended for medical oncologists, hematologistoncologists, gastrointestinal surgeons and other healthcare providers involved in the treatment of colorectal cancer (CRC).

OVERVIEW OF ACTIVITY

Cancer of the colon and rectum is the fourth most frequently diagnosed cancer and the second most common cause of death among all neoplasms in both men and women in the United States. Because of the high incidence and lethality of the disease, extensive clinical research has been undertaken in an attempt to find better treatments and possible cures. Unfortunately, in the past 5 years these efforts have yielded little in terms of new systemic therapeutic options for this disease.

However, an improved understanding of the biology of these tumors and the recent publication of several pivotal data sets have dramatically increased the collective enthusiasm that one day soon a number of new and effective therapies may be available to patients. To shed light on where we are and where we are headed with regard to the treatment of metastatic CRC (mCRC), these proceedings from a CME symposium at the 2013 ASCO Annual Meeting use the perspectives of clinical investigators to prepare clinicians for the impending introduction of potentially beneficial and exciting new strategies. By providing access to the latest research developments and expert opinions on this disease, this activity will assist medical oncologists and other healthcare providers in the formulation of up-to-date clinical management strategies for mCRC.

LEARNING OBJECTIVES

- Apply clinical research data to optimize the use of anti-VEGF- and anti-EGFR-based therapy in the long-term management of advanced CRC.
- Evaluate available research evidence with the use of regorafenib in mCRC, and identify potential patients in your practice for whom it might represent a reasonable nonprotocol option.
- Develop an evidence-based algorithm for the prevention and amelioration of side effects associated with chemother-

apeutic and biologic agents used in the management of mCRC.

- Individualize local and systemic treatment for patients with mCRC that is isolated to the liver.
- Recall new data with investigational agents demonstrating promising activity in CRC.
- Educate patients with synchronous colon or rectal cancer and metastatic disease on the benefits and risks associated with available up-front treatment options.

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Hardware/Software Requirements:

A high-speed Internet connection A monitor set to 1280 x 1024 pixels or more Internet Explorer 7 or later, Firefox 3.0 or later, Chrome, Safari 3.0 or later Adobe Flash Player 10.2 plug-in or later Adobe Acrobat Reader (Optional) Sound card and speakers for audio

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Douillard JY et al. Randomized, phase III trial of panitumumab with infusional fluorouracil, leucovorin, and oxaliplatin (FOLFOX4) versus FOLFOX4 alone as first-line treatment in patients with previously untreated metastatic colorectal cancer: The PRIME study. *J Clin Oncol* 2010;28(31):4697-705.

Heinemann V et al. Randomized comparison of FOLFIRI plus cetuximab versus FOLFIRI plus bevacizumab as first-line treatment of KRAS wild-type metastatic colorectal cancer: German AIO study KRK-0306 (FIRE-3). *Proc ASCO* 2013;Abstract 3506.

Oliner KS et al. Analysis of KRAS/NRAS and BRAF mutations in the phase III PRIME study of panitumumab (pmab) plus FOLFOX versus FOLFOX as first-line treatment (tx) for metastatic colorectal cancer (mCRC). *Proc ASCO* 2013;Abstract 3511.

Venook

Amado RG et al. Wild-type KRAS is required for panitumumab efficacy in patients with metastatic colorectal cancer. *J Clin Oncol* 2008;26:1626-34.

Douillard JY et al. Randomized, phase III trial of panitumumab with infusional fluorouracil, leucovorin, and oxaliplatin (FOLFOX4) versus FOLFOX4 alone as first-line treatment in patients with previously untreated metastatic colorectal cancer: The PRIME study. *J Clin Oncol* 2010;28(31):4697-705.

Karapetis CS et al. K-ras mutations and benefit from cetuximab in advanced colorectal cancer. *N Engl J Med* 2008;359(17):1757-65.

Maughan TS et al. Addition of cetuximab to oxaliplatin-based first-line combination chemotherapy for treatment of advanced colorectal cancer: Results of the randomised phase 3 MRC COIN trial. *Lancet* 2011;377(9783):2103-14.

Peeters M et al. Randomized phase III study of panitumumab with fluorouracil, leucovorin, and irinotecan (FOLFIRI) compared with FOLFIRI alone as second-line treatment in patients with metastatic colorectal cancer. *J Clin Oncol* 2010;28(31):4706-13.

Seymour MT et al. Addition of panitumumab to irinotecan: Results of PICCOLO, a randomized controlled trial in advanced colorectal cancer (aCRC). *Proc ASCO* 2011; Abstract 3523.

Tveit KM et al. Phase III trial of cetuximab with continuous or intermittent fluorouracil, leucovorin, and oxaliplatin (Nordic FLOX) versus FLOX alone in first-line treatment of metastatic colorectal cancer: The NORDIC-VII study. *J Clin Oncol* 2012;30(15):1755-62.

Van Cutsem E et al. Lessons from the adjuvant bevacizumab trial on colon cancer: What next? J Clin Oncol 2011;29(1):1-4.

Grothey

Corcoran RB et al. Pharmacodynamic and efficacy analysis of the BRAF inhibitor dabrafenib (GSK436) in combination with the MEK inhibitor trametinib (GSK212) in patients with BRAFV600 mutant colorectal cancer (CRC). *Proc ASCO* 2013;Abstract 3507.

Eng C et al. A randomized, placebo-controlled, phase I/II study of tivantinib (ARQ 197) in combination with cetuximab and irinotecan in patients (pts) with KRAS wild-type (WT) metastatic colorectal cancer (CRC) who had received previous front-line systemic therapy. *Proc ASCO* 2013; Abstract 3508.

Grothey A et al. Regorafenib monotherapy for previously treated metastatic colorectal cancer (CORRECT): An international, multicentre, randomised, placebo-controlled, phase 3 trial. *Lancet* 2013;381(9863):303-12.

Kopetz S et al. Phase II trial of infusional fluorouracil, irinotecan, and bevacizumab for metastatic colorectal cancer: Efficacy and circulating angiogenic biomarkers associated with therapeutic resistance. *J Clin Oncol* 2010;28(3):453-9.

Love N et al. Medical oncologists' clinical experiences and comfort levels with 20 recently approved agents. *Proc ASCO* 2013; Abstract e17570.

Mross K et al. A Phase I dose-escalation study of regorafenib (BAY 73-4506), an inhibitor of oncogenic, angiogenic, and stromal kinases, in patients with advanced solid tumors. *Clin Cancer Res* 2012;18(9):2658-67.

Schmoll HJ et al. ESMO Consensus Guidelines for management of patients with colon and rectal cancer: A personalized approach to clinical decision making. *Ann Oncol* 2012;23(10):2479-516.

Strumberg D et al. Regorafenib (BAY 73-4506) in advanced colorectal cancer: A phase I study. *Br J Cancer* 2012;21(6):879-89.

Wilhelm SM et al. Regorafenib (BAY 73-4506): A new multikinase inhibitor of angiogenic, stromal and oncogenic receptor tyrosine kinases with potent preclinical antitumor activity. *Int J Cancer* 2011;129(1):245-55.

Van Cutsem

Chua YJ, Cunningham D. Neoadjuvant treatment of unresectable liver metastases from colorectal cancer. *Clin Colorectal Cancer* 2006;5(6):405-12.

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

Kemeny N. Presurgical chemotherapy in patients being considered for liver resection. Oncologist 2007;12(7):825-39.

Leichman L. The role of chemotherapy in the curative treatment of patients with liver metastases from colorectal cancer. *Surg Oncol Clin N Am* 2007;16(3):537-56.

Leonard JP et al. Abbreviated chemotherapy with fludarabine followed by tositumomab and iodine I 131 tositumomab for untreated follicular lymphoma. *J Clin Oncol* 2005;23(24):5696-704.

Loupakis F. FOLFOXIRI plus bevacizumab (bev) versus FOLFIRI plus bev as first-line treatment of metastatic colorectal cancer (MCRC): Results of the phase III randomized TRIBE trial. Gastrointestinal Cancers Symposium 2013; Abstract 336.

Nordlinger B et al. EORTC liver metastases intergroup randomized phase III study 40983: Long-term survival results. *Proc* ASCO 2012; Abstract 3508.

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.

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.

Samalin E et al. Interim analysis of a multicenter phase II trial evaluating cetuximab in combination with FOLFIRINOX (LV5FU + irinotecan + oxaliplatin) as first-line treatment of metastatic colorectal cancer (mCRC) patients. Gastrointestinal Cancers Symposium 2008;Abstract 375.

Schmoll HJ et al. ESMO Consensus Guidelines for management of patients with colon and rectal cancer: A personalized approach to clinical decision making. *Ann Oncol* 2012;23(10):2479-516.

Schmoll HJ, Sargent D. Single agent fluorouracil for first-line treatment of advanced colorectal cancer as standard? *Lancet* 2007;370(9582):105-7.

Van Cutsem E et al. The diagnosis and management of gastric cancer: Expert discussion and recommendations from the 12th ESMO/World Congress on Gastrointestinal Cancer, Barcelona, 2010. Ann Oncol 2011;22(Suppl 5):1-9.

Van Cutsem E et al. Towards a pan-European consensus on the treatment of patients with colorectal liver metastases. *Eur J Cancer* 2006;42(14):2212-21.

Bekaii-Saab

Abbas S, Lam V. In colorectal liver metastases, the presence of extrahepatic disease correlates with the pathology of the primary tumour. *ISRN Oncol* 2011:948174.

Faron M et al. Impact on survival of primary tumor resection in patients with colorectal cancer and unresectable metastasis: Pooled analysis of individual patients' data from four randomized trials. *Proc ASCO* 2012; Abstract 3507.

Folprech G et al. Neoadjuvant treatment of unresectable colorectal liver metastases: Correlation between tumour response and resection rates. *Ann Oncol* 2005;16(8):1311-9.

McCahill LE et al. Primary mFOLFOX6 plus bevacizumab without resection of the primary tumor for patients presenting with surgically unresectable metastatic colon cancer and an intact asymptomatic colon cancer: Definitive analysis of NSABP trial C-10. *J Clin Oncol* 2012;30(26):3223-8.

Poultsides GA et al. Outcome of primary tumor in patients with synchronous stage IV colorectal cancer receiving combination chemotherapy without surgery as initial treatment. *J Clin Oncol* 2009;27(20):3379-84.

Primrose JN et al. A randomized clinical trial of chemotherapy compared to chemotherapy in combination with cetuximab in k-RAS wild-type patients with operable metastases from colorectal cancer: The new EPOC study. *Proc ASCO* 2013;Abstract 3504.

Wong SF et al. Primary tumor resection in metastatic colorectal cancer (mCRC): A prospective cohort study. *Proc ASCO* 2013; Abstract 3584.