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This is a CME activity that contains both audio and print components. To receive credit, the participant should listen to the CDs or tapes, review the monograph and complete the post-test and evaluation form. This monograph contains edited comments, clinical trial schemas, graphics and references which supplement the audio program and the website, **ColorectalCancerUpdate.com**, where you will find a full transcription of the audio program and an easy-to-use interactive version of this monograph with links to relevant full-text articles, abstracts, trial information and other web resources indicated here in **red underlined text**.

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Pharmaceutical agents discussed in this program

GENERIC	TRADE	MANUFACTURER
oxaliplatin	Eloxatin®	Sanofi-Synthelabo, Inc.
5-fluorouracil, 5-FU	--	Various manufacturers
leucovorin	--	Various manufacturers
cisplatin	Platinol®	Bristol-Myers Squibb Company
carboplatin	Paraplatin®	Bristol-Myers Squibb Company
capecitabine	Xeloda®	Roche Laboratories, Inc.
irinotecan	Camptosar®	Pharmacia Corporation

Editor's Note

Instructive Cases

A couple of years ago at ASCO, a community-based medical oncologist sitting next to me at a presentation commented, "Research leaders say one thing when they are on the podium, but I wonder what they really do with their own patients." Since that time, I have frequently asked researchers interviewed for our programs to present patients from their own practice. The results of these presentations have been fascinating.

In this program, Mace Rothenberg discusses a patient who sought his care because she wanted to be treated on a research protocol that included an anti-angiogenic agent. The patient, however, was too ill to meet the protocol entry criteria. After much discussion, the woman reluctantly agreed to take capecitabine and had an excellent response with minimal toxicity. Dr Rothenberg presented this case to a "consensus panel" and most of the respondents stated that they would have used multi-agent therapy. Dr Rothenberg believes that type of aggressive strategy would have been very risky in this patient with a poor performance status.

Additionally, James Cassidy presents a man in his 20s who had an excellent response to FOLFOX-4 (oxaliplatin/5-FU/leucovorin) followed by a two-staged complete hepatectomy. This was, in fact, the first time Dr Cassidy had ever employed this strategy, and at each step in this patient's complicated course, he and the patient agonized over how to proceed. Currently this man is not receiving active traditional therapy but is pursuing alternative medicine approaches.

These two cases are examples of the pitfalls of employing a "one-size-fits-all" approach to the treatment of patients with colorectal cancer. Research leaders interviewed for this series have repeatedly commented that the recent introduction of oxaliplatin, irinotecan and capecitabine have dramatically altered the therapeutic landscape and have thus made patients with courses like those of Drs Rothenberg and Cassidy much more common.

Ultimately, it seems likely that the greatest potential impact of these new agents and regimens will be in the adjuvant setting. Combined with the more widespread use of screening modalities like colonoscopy, these new additions to our armamentarium offer the possibility of a major step forward in colorectal cancer control.

— Neil Love, MD

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Edited comments by Dr Rothenberg

Development of oxaliplatin in the treatment of colorectal cancer

One of the primary reasons for the development of oxaliplatin in colorectal cancer is very provocative data from the laboratory looking at the NCI 60-human tumor cell line screen, where they looked at patterns of activity against different tumor types. They evaluated whether the concentration to inhibit 50 percent growth of those cell lines is average, above or below average for those 60 cell lines. Cisplatin and carboplatin have very little activity against the eight colorectal cancer cell lines and require higher-than-average concentrations to achieve that 50 percent inhibition. Oxaliplatin has a very different profile. In six of those eight colorectal cancer cell lines, it required lower-than-average concentrations to inhibit growth by 50 percent. These findings distinguish oxaliplatin as being not only structurally but also functionally different from the other platinum salts.

Potential role for oxaliplatin in overcoming 5-FU resistance

Oxaliplatin's interactions with other drugs, specifically 5-FU, may be one of the reasons we're seeing its activity in colorectal cancer. It may prevent one type of resistance mechanism seen in the laboratory and in patients. When cells upregulate thymidylate synthase (TS), they become less sensitive to 5-FU. Oxaliplatin reduces TS and may be resensitizing cells to inhibition by 5-FU. This may explain why patients respond to oxaliplatin/5-FU after progressing on frontline 5-FU alone.

Key recent and ongoing clinical trials with oxaliplatin

The natural evolution of oxaliplatin is already playing out. We've seen preliminary data from the NCCTG trial N9741 that showed a survival

advantage for FOLFOX-4 over IFL in the frontline setting. Oxaliplatin has also been moved to the adjuvant setting in the MOSAIC and NSABP trials. It's also being studied in conjunction with capecitabine to see whether or not there are advantages of not requiring a central venous catheter and whether oral therapy can give you the same kind of efficacy that we see with intravenous 5-FU therapy. There's going to be a lot of interest in that, and there are actually now several Phase II trials under development that will be looking at the capecitabine/oxaliplatin combination in various settings — first-line, second-line and the adjuvant setting.

Comparison of capecitabine/oxaliplatin (XELOX) versus FOLFOX

These Phase I/II trials are likely to be designed around equivalence. However, capecitabine is a more complicated drug than just an oral version of 5-FU. It actually has potential tumor selectivity, with thymidine phosphorylase (TP) being expressed at higher levels in tumor cells than normal cells. The more mature follow-up in trials using a capecitabine/oxaliplatin combination has shown very encouraging median survivals that are certainly in the ballpark, and maybe even higher than those that have been seen with infusional 5-FU and oxaliplatin combinations.

Improved survival due to newer chemotherapy agents

We will be debating the merits and shortcomings of the newer regimens for the foreseeable future, but we shouldn't lose sight of the fact that the median survival on these trials is now in the order of 18 to 20 months. When I was in medical school 20 years ago, the median survival for people with metastatic colorectal cancer was six months. It's hard to think of another common solid tumor where we've seen a tripling of the median survival in patients with metastatic disease, so all those drugs are important. Which one you use first versus which one you use second may not be as important as making sure that you integrate all those drugs into a treatment regimen.

Nonprotocol management of the patient with metastatic colorectal cancer

It's not a short visit with patients anymore. I can no longer say, "I'll give you 5-FU and see you in one week." How do we rationally combine the available agents in the individual patient's specific situation? I talk to them about the body of evidence that exists for infusional 5-FU given with irinotecan — a Douillard or FOLFIRI-type of regimen — showing a survival advantage over 5-FU. I would also talk about the FOLFOX regimen, showing an advantage over IFL. I tell them that those two regimens have been compared head-to-head in only one trial that showed it didn't matter which one you gave first; you got excellent overall survival with either one.

Next, I would tell them that we need an infusion catheter for each of those regimens. We'd talk about the side effects and that would help focus me on one regimen versus another. If a patient was more likely to be harmed because of a particular side effect, then that might make me lean in one direction with that patient and another direction for another patient.

Substituting capecitabine for infusional 5-FU

Oncologists often ask: Must we give 5-FU by infusion? Is capecitabine/oxaliplatin equivalent to 5-FU/oxaliplatin? My response is that capecitabine/oxaliplatin appears promising. I would not be able to say that capecitabine/oxaliplatin has definitively proven itself to be equivalent or superior to any other therapy. If there are some compelling reasons why some patients do not want a central venous catheter, and they understand that the data is Phase II — not Phase III data — and are comfortable with that level of uncertainty, then I treat those patients with capecitabine/oxaliplatin. I like to adhere to the gold standard, which is giving the drugs the way they were given in the clinical trial. If we are going to deviate from that, then patients need to be aware that there's a greater degree of uncertainty.

Select publications

Oxaliplatin in metastatic colorectal cancer

Becouarn Y et al. **Randomized multicenter phase II study comparing a combination of fluorouracil and folinic acid and alternating irinotecan and oxaliplatin with oxaliplatin and irinotecan in fluorouracil-pretreated metastatic colorectal cancer patients.** *J Clin Oncol* 2001;19(22):4195-201. **Abstract**

Cassinello J et al. **Multicenter phase II study of oxaliplatin (OXA) every two weeks in combination with weekly 5-FU bolus and folicic acid (FA) as first line treatment for advanced colorectal cancer (ACC).** *Proc ASCO* 2002; **Abstract 2244.**

Chau I et al. **Oxaliplatin and protracted venous infusion of 5-fluorouracil in patients with advanced or relapsed 5-fluorouracil pretreated colorectal cancer.** *Br J Cancer* 2001;85(9):1258-64. **Abstract**

Giacchetti S et al. **First line infusion of 5-fluorouracil, leucovorin, oxaliplatin for metastatic colorectal cancer chronomodulated versus conventional delivery. A multicenter randomized trial of the EORTC chronotherapy group.** *Proc ASCO* 2002; **Abstract 2231.**

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Grothey A et al. **Phase III study of bolus 5-fluorouracil (5-FU)/ folinic acid (FA) (Mayo) vs weekly high-dose 24h 5-FU infusion/ FA + oxaliplatin (OXA) (FUFOX) in advanced colorectal cancer (ACRC).** *Proc ASCO* 2002; **Abstract 512.**

Levi F et al. **Age-independent benefit of chronotherapy with 5-fluorouracil, leucovorin and oxaliplatin in patients with metastatic colorectal cancer within multicenter randomized phase III trials.** *Proc ASCO* 2002; **Abstract 1431.**

Ravaioli A et al. **Bolus fluorouracil and leucovorin with oxaliplatin as first-line treatment in metastatic colorectal cancer.** *J Clin Oncol* 2002;20(10):2545-50. **Abstract**

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Edited comments by Dr Cassidy

XELOX versus FOLFOX in metastatic disease

I tend to give XELOX (capecitabine and oxaliplatin). It's still early, but our own studies and others indicate that XELOX is as good as FOLFOX-4, but less toxic, much easier for the patient and without the complications of pumps and lines.

We've actually presented the Phase II data in 96 patients with a response rate greater than 50 percent, an additional 32 percent of patients with stable disease, decent progression-free survival and long overall survival. It's difficult to conceive that any two drug regimens available at the moment will be better than that.

The converse argument is: Why not irinotecan plus capecitabine? My answer is that this combination has not been examined quite as much as XELOX, so I would tend to go with that.

Reduction in neutropenia with capecitabine/oxaliplatin

There is a significant reduction in neutropenia with XELOX compared to what had been seen in other studies of FOLFOX. This may be due to patient selection, because of the small size of the study (only 96 patients). With this small number, even a handful of patients can change the rate of neutropenia. In addition, in this Phase II trial, the monitoring of neutropenia may not have been as strict. I'd like to see the raw data in order to actually be sure the events were real. However, I have no reason to suspect that the reduction in neutropenia is not real. If it is a real reduction in neutropenia, we begin to question whether a pharmacodynamic interaction could account for that.

Hand-foot syndrome with capecitabine alone and in combination with oxaliplatin

Only two percent of patients experienced grade 3 hand-foot syndrome with the XELOX combination, whereas hand-foot syndrome with single-agent capecitabine — albeit a slightly higher dose of 2500 mg/m^2 per day — is between 10 percent and 15 percent. This might suggest some interaction.

There is probably not a pharmacokinetic interaction, because this has been studied, but there could possibly be a pharmacodynamic difference. Oxaliplatin changes the expression of tumor enzymes, so a subtle pharmacodynamic change seen only with the combination is not inconceivable.

Phase III trial of XELOX versus FOLFOX in the metastatic setting

We are in the final stages of designing a large Phase III trial, which will randomize 1,000 patients with metastatic disease to XELOX versus FOLFOX-4. This trial will be an international effort, that we hope to get up and running very soon. There's a lot of interest in both FOLFOX-4 and XELOX, so I think centers and patients will sign on quickly.

I suspect that XELOX will be superior or equivalent, but with better patient tolerance and acceptability because of the oral administration. If we can achieve as much or more with capecitabine than 5-FU, I would see that as a bonus. Capecitabine is probably equivalent to infusional 5-FU in terms of efficacy and is a much easier treatment with probably less toxicity. Removing the pumps, lines and complications is a big step forward. If we can achieve that, I think XELOX will become one of the preferred first-line regimens for metastatic disease.

Capecitabine/oxaliplatin in the adjuvant setting

There is also going to be an adjuvant study of XELOX; however, neuropathy is not as acceptable in the adjuvant setting as it is in advanced disease. So I'm not entirely convinced that it will work out.

I think XELOX should be studied in the adjuvant setting, but my reticence is that we'll get some answers from the MOSAIC trial looking at 5-FU/folinic acid and oxaliplatin in the next two years. Perhaps we should wait to see if oxaliplatin is acceptable in terms of neurotoxicity. The disadvantage in waiting is that you delay everything by 18 months or two years.

Early evidence I have seen from an unpublished interim analysis of the MOSAIC trial is that there doesn't seem to be a major problem with neurotoxicity with adjuvant oxaliplatin. Of course, "the devil is in the details," and we don't know how many patients actually received all the oxaliplatin they were scheduled to receive, how many dropped out, how many got neuropathy, how many recovered from neuropathy and how many have long-term neuropathy. These details will take a while to come out.

I would still be very happy to take part in the clinical trial because I think it will be an effective regimen, however, the trade-offs are important in the adjuvant setting.

Substituting capecitabine for 5-FU

I hope we don't need to test in a randomized clinical trial every time we substitute capecitabine for 5-FU. I would like to think that we could show that conceptually this has been done in breast cancer, colon cancer and perhaps one other tumor. If you could show this phenomenon happening three times, how many more times do you really need to test it?

Select publications

Oxaliplatin in metastatic colorectal cancer

Borner MM et al. **Phase II study of capecitabine and oxaliplatin in first- and second-line treatment of advanced or metastatic colorectal cancer**. *J Clin Oncol* 2002;20(7):1759-66. **Abstract**

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Hobday TJ et al. **Perspectives on the role of sequential or combination chemotherapy for first-line and salvage therapy in advanced colorectal cancer.** *Clin Colorectal Cancer* 2002;2(3):161-9. **Abstract**

Jordan K et al. **Randomized phase II trial of capecitabine plus irinotecan vs capecitabine plus oxaliplatin as first-line therapy in advanced colorectal cancer (ACRC): Results of an interim analysis.** *Proc ASCO* 2002; **Abstract 2225.**

Kondo Y et al. **A multicenter phase II trial of capecitabine (Xeloda™) in previously untreated advanced/metastatic colorectal cancer.** *Proc ASCO* 2002; **Abstract 2322.**

Kovcin VN et al. **First line capecitabine (Xeloda) chemotherapy for metastatic colorectal cancer (MCRC) in patients with liver dysfunction.** *Proc ASCO* 2002; **Abstract 2379.**

Lersch C et al. **Prevention of oxaliplatin-induced peripheral sensory neuropathy by carbamazepine in patients with advanced colorectal cancer.** *Clin Colorectal Cancer* 2002;2(1):54-8. **Abstract**

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Rothenberg ML. **Current status of capecitabine in the treatment of colorectal cancer.** *Oncology (Huntington)* 2002;16(12 Suppl No 14):16-22. **Abstract**

Shields AF et al. **A phase II trial of oxaliplatin and capecitabine in patients with advanced colorectal cancer.** *Proc ASCO* 2002; **Abstract 568.**

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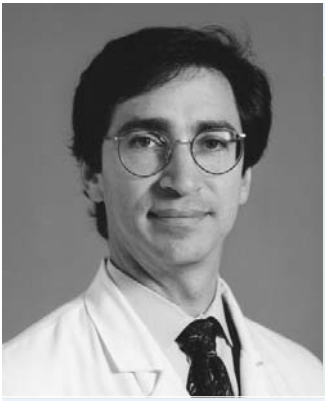
Wein A et al. **Neoadjuvant treatment with weekly high-dose 5-fluorouracil as 24-hour infusion, folinic acid and oxaliplatin in patients with primary resectable liver metastases of colorectal cancer.** *Oncology* 2003;64(2):131-8. **Abstract**

Yang TS et al. **Biweekly bolus 5-fluorouracil and leucovorin plus oxaliplatin in pretreated patients with advanced colorectal cancer: A dose-finding study.** *Anticancer Drugs* 2003;14(2):145-51. **Abstract**



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Edited comments by Dr Saltz

Clinical issues raised by Intergroup N9741

Intergroup N9741 raised a number of questions, including the use of bolus versus infusional fluorouracil. In that trial, the control arm was the IFL regimen (bolus irinotecan/fluorouracil/leucovorin). The investigational arm was the FOLFOX-4 regimen, which is two 22-hour fluorouracil infusions with leucovorin infusions in the middle with oxaliplatin. So we've got two variables — irinotecan versus oxaliplatin, and fluorouracil bolus versus fluorouracil infusion. In that study, the overall survival, time to tumor progression and response rate were superior for the FOLFOX arm. However, there are some confounding issues that make it difficult to know how to put those data into context.

One study that helps us was reported at ASCO in 2001 by Christopher Tournigand. This evaluated oxaliplatin versus irinotecan without varying the fluorouracil. So, all patients got the same biweekly fluorouracil/leucovorin, and the variable was whether they got oxaliplatin or irinotecan. All patients were planned for a crossover; as soon as they failed on one, they went onto the other. In that study, the survival of the two arms as well as the time to tumor progression of the first-line and second-line regimen are virtually identical, and response rates to first line are identical.

The study is underpowered, with only about 110 patients in each arm, but when you look at the survival curve it is very hard to be convinced that a larger study would have shown a significant divergence. This suggests that when used with infusional fluorouracil, the choice can be irinotecan or oxaliplatin. The safety profiles with the infusional, biweekly regimen appeared to be easier for patients to tolerate, and for doctors to deal with, because fewer dose modifications were required.

Application of clinical trial results to practice

Either regimen of irinotecan/fluorouracil/leucovorin or oxaliplatin/fluorouracil/leucovorin would be an appropriate first-line consideration, and those are my current default positions when I see patients outside of a clinical trial. I am routinely recommending that they have an indwelling catheter inserted and that we treat them with a biweekly fluorouracil infusion plus either irinotecan or oxaliplatin. We discuss the relative merits and downsides to each drug. Since I'm not convinced there are efficacy data to help us select one over the other, I talk to patients about the different side-effect profiles. For patients where GI toxicity or loss of hair is going to be particularly problematic, oxaliplatin-based therapy is better. For patients where neurotoxicity could be particularly problematic, irinotecan is a better choice.

Use of tumor markers in postsurgical management

Oftentimes I'll be asked whether or not a tumor marker should dictate a major change in therapy; I'm not a believer in doing that. Tumor markers are overused in this country. They do provide some information, but they are an indication to look more carefully, not necessarily to act. For example, I do not advocate the initiation of therapy due to a bump in CEA where you can't find any evidence of tumor any other way. I do not advocate changing a therapy if the CEA starts going up or abandoning a therapy if the CEA doesn't go down. I look at how the patient is doing, I look at the CAT scan or MRI evidence, and that is what tends to help me make my decisions. In very borderline situations a significant movement of CEA may color my decision, but in general I don't advocate making major therapeutic decisions on the basis of a marker. I haven't found markers other than CEA to be particularly helpful in colorectal cancer and I don't routinely obtain them.

Select publications

The use of tumor markers in the postsurgical management of colorectal cancer

Bast RC Jr et al. **2000 update of recommendations for the use of tumor markers in breast and colorectal cancer: Clinical practice guidelines of the American Society of Clinical Oncology.** *J Clin Oncol.* 2001;19(6):1865-78. **Abstract**

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Duffy MJ. **Carcinoembryonic antigen as a marker for colorectal cancer: Is it clinically useful?** *Clin Chem* 2001;47(4):624-30. **Abstract**

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Kievit J. **Follow-up of patients with colorectal cancer: Numbers needed to test and treat.** *Eur J Cancer* 2002;38(7):986-99. **Abstract**

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Edited comments by Dr Tebbutt

Phase III study comparing capecitabine with fluorouracil and oxaliplatin with cisplatin in patients with advanced esophagogastric cancer

Trial background, rationale and design

This study builds upon the epirubicin/cisplatin/5-FU (ECF) regimen devised by David Cunningham's group in the GI units of the Royal Marsden Hospital. Importantly, this regimen uses a protracted venous infusion (PVI) schedule of 5-FU, which is not as myelosuppressive as bolus schedules of 5-FU.

The rationale for the ECF regimen was that, while these three agents don't have single-agent activity in the adjuvant setting for esophagogastric cancer, by putting them together you've got three agents with independent activity and nonoverlapping toxicity profiles. This regimen went through initial Phase II trials, showing significant activity. There have now been two large randomized studies establishing ECF as a highly active regimen, which is a standard of care in the United Kingdom, many parts of Europe and Australia.

This study examines the role of capecitabine and oxaliplatin in bringing the ECF regimen forward. Capecitabine is an oral treatment, without the hassles and complications of lines and pumps. The other potential advantage of capecitabine is the fact that it is activated via thymidine phosphorylase, which itself is upregulated by other agents. So, there is potential for synergy by combining capecitabine with other agents, which activate thymidine phosphorylase.

Oxaliplatin has activity in a variety of cisplatin-resistant tumors, and generally has a more favorable toxicity profile than cisplatin. There is less renal toxicity, and patients do not need the same prehydration with oxaliplatin that they need with cisplatin. There is also less auditory toxicity and neurotoxicity.

The study was designed to establish the role of those two agents — capecitabine and oxaliplatin — building from the ECF regimen. It's a 2-by-2 factorial design, with essentially two randomizations: cisplatin or oxaliplatin, and PVI 5-FU or capecitabine.

Randomised, Multicentre Phase III Study Comparing Capecitabine with Fluorouracil and Oxaliplatin with Cisplatin In Patients with Advanced Oesophago-Gastric Cancer

ARM 1	Epirubicin + cisplatin + fluorouracil (ECF)
ARM 2	Epirubicin + oxaliplatin + fluorouracil (EOF)
ARM 3	Epirubicin + cisplatin + capecitabine (ECX)
ARM 4	Epirubicin + oxaliplatin + capecitabine (EOX)

DERIVED FROM: Tebbutt N et al. **Randomised, multicentre phase III study comparing capecitabine with fluorouracil and oxaliplatin with cisplatin in patients with advanced oesophago-gastric cancer: Interim analysis.** *Proc ASCO* 2002; **Abstract 523.**

Interim study results

Currently accrual stands at about 200 patients, with a targeted accrual of 600. I presented a planned interim analysis after 80 patients, but it's difficult to make significant interpretations. All the regimens, and importantly the two experimental regimens, look active. The study is designed to compare the 5-FU treatment arms with the capecitabine treatment arms separately. Response rates and toxicity results in the two experimental arms are very promising.

The toxicity results were no worse for the capecitabine treatment arms, and they certainly looked better than the toxicity encountered with PVI 5-FU. But, this is a randomized Phase II trial, and we can't interpret too much. When the study is completed, we will be able to very confidently define the role of capecitabine and oxaliplatin in upper GI cancer.

Efficacy and tolerability of a Phase III study comparing capecitabine with fluorouracil and oxaliplatin with cisplatin in patients with advanced oesophago-gastric cancer

	Fluorouracil versus Capecitabine		Cisplatin versus Oxaliplatin	
	ECF + EOF	ECX + EOX	ECF + ECX	EOF + EOX
# patients	38	40	35	43
Median age (yrs)	61	63	60	64
CR + PR (95% CI)	22% (9-42)	49% (31-66)	37% (20-56)	38% (21-56)
Grade 3/4 diarrhea	14%	3.2%	3.7%	12.5%
Grade 3/4 stomatitis	3.6%	0%	0%	3.1%
Grade 3/4 PPE	3.6%	3.2%	7.4%	0%
Grade 3/4 neutropenia	32%	40%	34%	38%
Febrile neutropenia	3.6%	3.2%	3.7%	3.1%

E=epirubicin 50 mg/m^2, C=cisplatin 60 mg/m^2, F= fluorouracil 200 mg/m^2
O=oxaliplatin 130 mg/m^2, X=capecitabine 1000 mg/m^2

DERIVED FROM: Tebbutt N et al. **Randomised, multicentre phase III study comparing capecitabine with fluorouracil and oxaliplatin with cisplatin in patients with advanced oesophago-gastric cancer: Interim analysis.** *Proc ASCO* 2002; **Abstract 523.**

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Post-test

02-1246-ES-12 CCU1 | 2003

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Bridging the Gap between Research and Patient Care

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Name: _____

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

Signature: _____

Questions *(please circle answer)*:

1. A mechanism by which oxaliplatin may prevent or reverse resistance to 5-FU is:
- a. downregulating thymidylate synthase (TS)
- b. upregulating thymidylate synthase
- c. eliminating intratumoral thymidine phosphorylase (TP)
- d. nonexistant; oxaliplatin has no effect on 5-FU resistance

2. After 12 doses of oxaliplatin 85 mg/m^2 (total dose 1020 mg/m^2), approximately what percentage of patients will have developed cumulative neurotoxicity?
- a. less than 10%
- b. 15%-20%
- c. 40%
- d. Over 60%

3. In approximately 50% of patients, cumulative neurotoxicity from oxaliplatin will resolve completely.
- a. True
- b. False

4. In the Intergroup N9741 clinical trial, overall survival was superior for:
- a. bolus irinotecan/fluorouracil/leucovorin (IFL)
- b. oxaliplatin plus infusional fluorouracil/leucovorin (FOLFOX-4)
- c. oxaliplatin plus irinotecan

5. Which of the following is a major dose-limiting side effect of irinotecan (CPT-11)?
- a. diarrhea
- b. neuropathy
- c. pharyngolaryngeal dysesthesia
- d. asthenia

6. The combination of oral capecitabine plus oxaliplatin (XELOX) is being evaluated in:
- a. first-line metastatic setting
- b. adjuvant setting
- c. a and b

7. There may be less hand-foot syndrome in the XELOX regimen compared to single-agent capecitabine.
- a. True
- b. False

8. Which of the following are potential advantages of incorporating capecitabine and oxaliplatin into the ECF regimen (epirubicin/cisplatin/protracted venous infusion of 5-FU)?
- a. oral therapy versus infusional
- b. potential upregulation of TP
- c. more favorable toxicity profile
- d. all of the above

Post-test Answer Key: 1.b, 2.b, 3.a, 4.b, 5.a, 6.c, 7.a, 8.d

To obtain a certificate of completion and receive credit for this activity, please complete the post-test, fill out the evaluation form and mail or fax both to: Postgraduate Institute for Medicine, P. O. Box 260620, Littleton, CO 80163-0620, FAX (303) 790-4876. You may also complete the Post-test and Evaluation online at www.ColorectalCancerUpdate.com/CME.

Evaluation Form

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Postgraduate Institute for Medicine (PIM) respects and appreciates your opinions. To assist us in evaluating the effectiveness of this activity and to make recommendations for future educational offerings, please take a few minutes to complete this evaluation form. Please note, a certificate of completion is issued only upon receipt of your completed evaluation form.

Please answer the following questions by circling the appropriate rating:
5 = *Outstanding* 4 = *Good* 3 = *Satisfactory* 2 = *Fair* 1 = *Poor*

Global Learning Objectives
Upon completion of this activity, participants should be able to:

- Describe ongoing clinical trials in colorectal cancer and their potential impact on patient care. 5 4 3 2 1
- Critically evaluate the clinical implications of emerging clinical trial data in colorectal cancer treatment. 5 4 3 2 1
- Develop and explain a management strategy for patients with colorectal cancer in the adjuvant and metastatic settings. 5 4 3 2 1

Specific Learning Objectives for Issue 1
Upon completion of this activity, participants should be able to:

- Describe the efficacy and side effects of oxaliplatin and irinotecan in combination with bolus and infusional 5-FU/leucovorin regimens and capecitabine to individualize chemotherapy in patients with colorectal cancer. 5 4 3 2 1
- Explain how patient and treatment characteristics influence choice of chemotherapy regimen in colorectal cancer. 5 4 3 2 1
- Evaluate new data incorporating capecitabine and oxaliplatin into the ECT regimen for esophagogastric cancer in order to determine the application of these data to patient care. 5 4 3 2 1

Overall effectiveness of the activity

Objectives were related to overall purpose/goal(s) of activity 5 4 3 2 1
Related to my practice needs 5 4 3 2 1
Will influence how I practice 5 4 3 2 1
Will help me improve patient care 5 4 3 2 1
Stimulated my intellectual curiosity 5 4 3 2 1
Overall quality of material 5 4 3 2 1
Overall, the activity met my expectations 5 4 3 2 1
Avoided commercial bias or influence 5 4 3 2 1

Will the information presented cause you to make any changes in your practice? ___Yes ___No

If Yes, please describe any change(s) you plan to make in your practice as a result of this activity.

What other topics would you like to see addressed in future educational programs?

Degree:

☐ MD ☐ DO ☐ PharmD ☐ RN ☐ NP ☐ PA ☐ BS ☐ Other _____