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Colorectal Cancer Drugs Require Careful Patient Selection

Patients with advanced colorectal cancer who have mutant forms of the gene *KRAS* in their tumors should not receive chemotherapy plus cetuximab (Erbitux), because they are unlikely to benefit from the treatment and should be spared the side effects and cost, researchers said at the recent American Society of Clinical Oncology (ASCO) annual meeting in Chicago.

Based on a growing body of evidence, including findings presented at the meeting, several experts predicted that it will become standard practice to test all colorectal tumors for mutations in the *KRAS* gene before starting patients with advanced disease on therapies involving cetuximab and a similar drug, panitumumab (Vectibix).

"I believe it is now warranted to test all patients being considered for these agents," said Dr. Gail Eckhardt of the University of Colorado Denver, who was not involved in the research and discussed the findings at ASCO. "Patients with *KRAS* mutations should not receive cetuximab or panitumumab in [certain] settings."

These drugs are designed to block the activity of the epidermal growth factor receptor (EGFR) protein, which is often overactive in colorectal cancer.

An estimated 30 to 40 percent of colorectal tumors carry *KRAS* mutations, and commercial tests are available. Screening could proceed based on the breast cancer model, where women undergo testing for genetic characteristics of their tumors prior to treatment with trastuzumab (Herceptin).

"*KRAS* is the first molecular marker for targeted therapy in combination with standard chemotherapy as a

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Cancer Research Highlights

Gemcitabine After Pancreatic Cancer Surgery Improves Survival

Patients who received the chemotherapy drug gemcitabine after surgery for pancreatic cancer lived 2 months longer than patients who had surgery alone, according to the final results of a large, randomized clinical trial presented at the ASCO annual meeting last week.

Less than 20 percent of patients with pancreatic cancer are candidates for surgery, because the disease is often detected in the late stages. Gemcitabine has been a standard treatment for patients with advanced (and inoperable) pancreatic cancer for a decade. The new findings support use of the drug in the adjuvant setting.

"We have shown that this treat-

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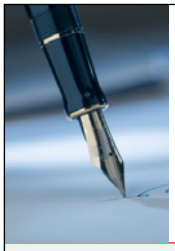

Director's Update

On May 31, NCI Director Dr. John Niederhuber delivered remarks during the opening session of the 2008 Annual Meeting of the American Society of Clinical Oncology (ASCO) in Chicago, Illinois. To read his remarks, please visit the HTML version here: http://www.cancer.gov/ncicancerbulletin/NCI_Cancer_Bulletin_061008/page4. ◆

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first-line treatment for metastatic colorectal cancer," said Dr. Eric Van Cutsem of Gasthuisberg University Hospital in Leuven, Belgium, at the meeting. "If we know in advance that a patient has a *KRAS* mutation, then we know we don't have to treat the patient [with these agents]."

He presented new results from the CRYSTAL trial, which last year showed that some patients with metastatic disease benefited from cetuximab plus chemotherapy with respect to progression-free survival. But not all patients benefited and given growing interest in the *KRAS* gene, the researchers went back and looked at tumor tissue from 587 of the nearly 1,200 patients in the trial.

The results were striking: Only patients with normal *KRAS* genes benefited. Perhaps most important, findings from other studies, including the OPUS and EVEREST trials, support the findings from the CRYSTAL trial. Retrospective analyses of *KRAS* gene status and treatment outcomes have now been performed on 1,200 patients with advanced colorectal cancer from separate randomized trials.

"We now have substantial evidence that mutations in *KRAS* are a negative predictive marker for the use of cetuximab with chemotherapy and for panitumumab as a single agent based on results from a variety of trials," said Dr. Margaret Mooney of NCI's Cancer Therapy Evaluation Program, who was not involved in the research.

Before the meeting, European regulators approved cetuximab plus chemotherapy as a first-line treatment for colorectal cancer in patients with normal *KRAS*. Panitumumab is approved in Europe for treating advanced colorectal cancer, but also only in patients with the normal *KRAS* gene.

Prospective studies are now needed to validate the marker. Trials such as CRYSTAL were not designed to answer questions about cetuximab and *KRAS*, and the researchers do not have tumor tissue from all patients. These patients could provide useful information in developing new therapies.

Dr. Eckhardt stressed the importance of communicating to patients with *KRAS* mutations that current chemotherapy regimens are effective. "Hopefully," she added, this is "only the beginning of the era of individualized therapy for patients with colon cancer." ◆

By Edward R. Winstead

(Highlights continued from page 1)

ment more than doubles the overall survival 5 years after treatment," said Dr. Helmut Oettle of the Charité School of Medicine in Berlin, Germany, who presented the results.

The study included 368 patients who underwent surgery followed by 6 months of adjuvant gemcitabine treatment or surgery alone. In the gemcitabine group, 21 percent were alive at 5 years compared with 9 percent in the control group. Median survival in the gemcitabine group was 22.8 months compared with 20.2 months in the control group.

Preliminary results from the trial were reported at ASCO in 2005 and showed that post-surgery gemcitabine could delay a recurrence of the disease. These findings led to an increase in the use of the drug in the United States and Europe, according to the researchers.

"We can now say that giving this agent after surgery to patients with early stage disease will improve a patient's survival," commented Dr. Nicholas Petrelli of the Helen F. Graham Cancer Center at the meeting. "We couldn't say that before."

Cetuximab Plus Chemotherapy Extends Survival for Advanced Lung Cancer

Patients with advanced non-small-cell lung cancer (NSCLC) who received cetuximab (Erbitux) plus chemotherapy lived on average 5 weeks longer than patients who received chemotherapy alone, according to results reported at the ASCO annual meeting.

In the phase III FLEX trial, 1,125 patients with all types of NSCLC were randomly assigned to receive

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Cancer Research Highlights

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standard platinum-based chemotherapy alone or chemotherapy plus cetuximab. Nearly all of the patients had stage IV disease. Overall survival was higher for those who received cetuximab plus chemotherapy (11.3 months) compared with those who received chemotherapy alone (10.1 months).

The benefit of the combination therapy was seen in patients with all histological subtypes of NSCLC, including adenocarcinoma and squamous cell carcinoma, the two most common subtypes. The main side effect was an acne-like skin rash that could be managed.

"Patients with advanced NSCLC have limited treatment options and life expectancy is short, so the survival increase shown in this study is an important step for these patients," noted Dr. Robert Pirker, an associate professor of medicine at the Medical University of Vienna in Austria and the study's lead author.

The only other final-stage randomized trial to show a survival benefit in lung cancer was a 2005 study of bevacizumab (Avastin) plus chemotherapy. Unlike the current study, that trial did not include patients with squamous cell carcinoma.

Dr. Thomas Lynch of Massachusetts General Hospital, who commented on the findings at ASCO, said the study was well done and produced "a clinically meaningful benefit for a large population."

Zoledronic Acid Improves Early Breast Cancer Treatment

The addition of zoledronic acid (Zometa) to adjuvant endocrine therapy in premenopausal women with early stage breast cancer significantly improves clinical outcomes beyond those achieved with endocrine therapy alone, researchers reported at the ASCO annual meeting. The results are from a phase III randomized trial of 1,800 women conducted by the Austrian Breast and Colorectal Cancer Study Group.

Zoledronic acid, part of a class of drugs known as bisphosphonates, is already used to treat bone metastases, and this trial was conducted based on data from preclinical and early phase trials indicating that the drug can also shrink tumors and block metastatic activity. The results bear this out, said principal investigator Dr. Michael Gnant from the Medical University of Vienna.

Overall, the trial showed no difference in disease-free survival between women treated with tamoxifen or anastrozole. But the addition of zoledronic acid to either therapy decreased the risk of a disease-free survival event by 36 percent compared with hormone therapy alone, Dr. Gnant said. At a median follow-up of 60 months, overall disease-free survival was 92.4% and overall survival was 97.7%.

Women in the trial—all of whom were premenopausal with stage I or II breast cancer that was responsive to endocrine therapy—were treated with surgery and, if needed, radiation therapy. They also received the drug goserelin to temporarily suppress the function of the ovaries. Each was randomly assigned to one of four adjuvant therapy arms: tamoxifen alone, the aromatase inhibitor anastrozole alone, or either drug plus zoledronic acid. Treatment lasted 3 years.

The drug was also well tolerated, with no indication of increased risk of liver problems or damage to the jaw bone—two side effects which have been associated with higher doses of bisphosphonate drugs.

Acupuncture Tested in Cancer Patients after Neck Surgery

For patients with head and neck cancers who undergo a surgical procedure known as neck dissection, acupuncture may help reduce pain and improve functioning afterward, according to preliminary findings from a randomized trial presented as a poster at ASCO.

"Acupuncture appears to be a promising treatment for these patients, and more research is warranted," said Dr. David Pfister of Memorial Sloan-Kettering Cancer Center, who discussed the results at ASCO. Conventional treatments have limited success in helping patients following neck dissections, he noted, and "there is plenty of room for improvement."

The study included 34 patients who received acupuncture and 36 who received standard care with pain medication and physical therapy. In the experimental group, four sessions of acupuncture were administered over the course of a month. A standard set of acupuncture points was used for each patient, and more specialized points were selected depending on the pain for each individual.

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(Highlights continued from page 3)

Thirty-nine percent of the patients who received acupuncture had significant improvements in pain and function, compared with only 7 percent who experienced improvement in the standard care group, according to assessments using a measure called the Constant-Murley scale. Some patients in the acupuncture group had significant relief of dry mouth, while no relief was observed in the patients receiving standard care.

Future studies may include a group that receives "sham" acupuncture to control for the placebo effect.

Protein Biomarkers Point to Early Stage Pancreatic Cancer

Researchers have discovered proteins in blood that reliably indicate early stage pancreatic cancer, according to a report June 10 in *PLoS Medicine*. Although more research is needed before an actual diagnostic test could be developed, the study's lead author, Dr. Samir Hanash from the Fred Hutchinson Cancer Research Center, said the study represents a "breakthrough in the application of advanced proteomic technologies and mouse models to cancer-biomarker discovery."

The mouse model used in the study was genetically engineered to mimic the course of pancreatic cancer in humans, from development of precancerous lesions through advanced disease. Using proteomic technologies, the researchers identified a panel of five proteins—LCN2, REG1A, REG3, TIMP1, and IGFBP4—consistently found in mice with precancerous growths called pancreatic intraepithelial neoplasia, but not in mice with full-blown cancer or healthy control mice.

To validate the five-protein panel, they tested it against blood samples from 13 people in an unrelated cancer prevention study who developed pancreatic cancer within a year of donating the sample. The researchers were "blinded" to which samples came from cancer patients and controls. The five-protein panel consistently identified samples from the patients who developed cancer, and when it was combined with another protein marker, CA19.9, which is elevated in up to 80 percent of newly diagnosed pancreatic cancer patients, the test was even more accurate.

The next steps include studies to validate the biomarker panel's performance in distinguishing between pancreatitis (inflammation of the pancreas) and pancreatic cancer—under the auspices of NCI's Early Detection Research Network (which also partly funded this current study, along with NCI's Mouse Models of Human Cancers Consortium)—and continued studies to assess its value in early detection among those at high risk of pancreatic cancer.

Initial Costs of Cancer Treatment on the Rise

In the first study to examine trends in the costs of specific components of initial cancer care in the United States, investigators found that Medicare payments for initial treatment rose significantly for breast, colorectal, and lung cancer patients but dropped slightly for prostate cancer patients between 1991 and 2002. These results, published online June 10 in the *Journal of the National Cancer Institute*, highlight the financial challenges to Medicare posed by the rising number of cancer patients in the United States as the population ages, the study authors said.

The investigators used the linked Surveillance, Epidemiology, and End Results-Medicare data from 306,709 newly diagnosed breast, colorectal, lung, and prostate cancer patients age 65 or older. Specific services evaluated included cancer-related surgery, chemotherapy, radiation therapy, and hospitalizations during the initial treatment period (defined as from 2 months prior to 12 months following diagnosis). The investigators assessed the proportion of patients who were hospitalized, received cancer-related surgery, chemotherapy, and radiation therapy, as well as the average cost per patient for those services.

After adjusting for inflation, the investigators found that between 1991 and 2002 the average cost per patient rose $7,139, $5,345, and $4,189 for lung, colorectal, and breast cancer, respectively. Prostate cancer costs decreased by $196, due to a decline in the use of radical prostatectomy. The most significant increases were due to the percentage of breast, lung, and colorectal cancer patients receiving chemotherapy and the average cost per patient for chemotherapy. Over this time period the proportion of breast and prostate cancer patients receiving radiation therapy increased, as did the cost of radiation therapy. However, hospitalizations during the initial treatment period accounted for the greatest portion of total Medicare payments.

The study ended before the introduction of new, more expensive chemotherapies and targeted therapies such as erlotinib and bevacizumab, noted the authors. "Evaluation of the impact of these new agents on total Medicare expenditures for initial cancer care will be a priority for future research," said the lead author, Dr. Joan Warren from NCI's Division of Cancer Control and Population Sciences. ◆

Spotlight

Ovarian Cancer Study Could Speed Early Detection

Can a simple blood test detect early signs of ovarian cancer? This question has been asked repeatedly over the last decade, and an answer may finally come this summer.

Nearly 3 million specimens, including prediagnostic blood samples from women with ovarian cancer are stored at the Prostate, Lung, Colorectal, and Ovarian (PLCO) Biorepository, in Frederick, MD.

In a closely watched study, five research groups are validating their most promising ovarian cancer markers using high-quality blood samples from the Prostate, Lung, Colorectal and Ovarian (PLCO) cancer screening trial, including some prediagnostic samples from women who developed ovarian cancer during the trial.

The validation study, coordinated by NCI's Early Detection Research Network (EDRN), could show whether panels of markers can detect ovarian cancer in blood collected 6 months or more before cancer was discovered. If markers do predict ovarian cancer, the question then becomes: How long before a clinical diagnosis are the markers informative?

Earlier is always better, and for this disease in particular. Ovarian cancer has been called a "silent killer" because the vast majority of cases go undetected until the later stages, when women have few treatment options. The hope now is that a blood test for early detection is within reach.

"Everybody has a real sense of urgency now," said Dr. Daniel Cramer of Brigham and Women's Hospital, who leads one group. "We've been saying for years that we'll get a marker for ovarian cancer, but it hasn't happened yet. This is the first good test to see if we can come up with a panel of markers for ovarian cancer from PLCO samples."

The PLCO is one of several large, randomized studies that have been making limited samples available for biomarker research based on proposals from investigators. These studies have rare prediagnostic samples that were collected before anyone knew that a person had a particular cancer. Such samples are considered "more pure" and may more accurately reflect the biology of ovarian cancer than other specimens.

The vast majority of prediagnostic blood samples for ovarian cancer are collected from women just prior to surgery for a suspected ovarian tumor. But impending surgery and anesthesia, for example, might alter at least some potential markers in women with the cancer but perhaps not in a comparison group.

The PLCO biorepository has serial blood samples from 150,000 people collected at 10 sites across the country, making it a veritable gold mine for biomarker research. Because samples were collected and stored before a diagnosis was known, the researchers minimized the chances of inadvertently introducing a bias or systematic difference between the cancer and comparison groups.

Similarly, in the validation study, great care was taken to eliminate factors that, in the end, could mislead investigators.

"If the biomarkers do not detect ovarian cancer in these samples, it will be because of the biology of ovarian cancer and not because of how the study was designed or implemented," said Dr. Christine D. Berg of NCI's Division of Cancer Prevention and the leader of PLCO.

The validation study is being managed by Dr. Christos Patriotis of NCI's Cancer Biomarkers Research Group with Dr. Sudhir Srivastava, who heads the EDRN program.

The study could yield a variety of markers, including some that improve the sensitivity of the protein CA-125 test. This marker is routinely evaluated when diagnosing ovarian

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cancer, but it cannot be used alone because only some women with ovarian cancer develop elevated levels, and levels can be elevated for reasons other than cancer.

"Many potential biomarkers have been proposed to be added to CA-125 for the early detection of ovarian cancer, and the PLCO samples will help us select the most promising of those markers," said Dr. Robert Bast, Jr., of the University of Texas M.D. Anderson Cancer Center, who discovered CA-125 and is an investigator in the study.

"A lot of people around the country are holding their breath to see the results.... If the results are positive in these samples, it will be enormously good news for the field."

Beyond early detection and diagnosis, markers are needed to assess risk and guide difficult clinical decisions. For instance, some women with genetic risk factors for breast and ovarian cancers have their ovaries and fallopian tubes removed as preventive measures after childbearing years.

The validation study could yield markers that identify women without the risk genes who nonetheless have a high risk of the disease within 5 to 10 years. Other markers could identify women who have a family history of ovarian cancer but are at such low risk that they could safely avoid preventive surgeries, at least in the short term.

Before any of these markers can be used in the clinic, they would need to be tested prospectively, and the challenges of early detection are substantial.

"It may be helpful to think about what we're trying to do," said Dr. Nicole Urban of Fred Hutchinson Cancer Research Center, another lead investigator. "With a screening program, a woman comes in and you get a blood sample and try to predict if she's going to be diagnosed with cancer. You're trying to find cancer that would kill the woman, but you're trying to find it early enough that you can cure it. And this is tough."

Dr. Urban is nonetheless optimistic that screening for ovarian cancer using markers will ultimately succeed. She predicts that serial blood samples from randomized trials may be required to discover the markers and track their changes over time.

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FDA Update

FDA Conducting Safety Review of TNF Blockers, Adds Warning to Becaplermin

The Food and Drug Administration (FDA) is investigating the possible association between drugs known as tumor necrosis factor (TNF) blockers and the development of several cancers, primarily lymphomas. The drugs—sold in the United States as Remicade, Enbrel, Humira, and Cimzia—are used to treat children and young adults for juvenile idiopathic arthritis and Crohn disease, as well as other diseases, FDA explained in an "early communication" about the investigation.

The review follows 30 reports of cancer in children and young adults (age 18 or under) submitted via the agency's Adverse Event Reporting System since 1998, when the first TNF blocker was approved. Of the cancers reported, FDA said, approximately half were lymphomas, including Hodgkin and non-Hodgkin lymphoma.

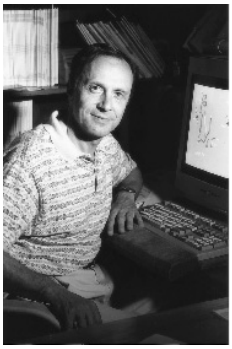
"While cancers are known to occur in children and young adults, the reports of these events in children and young adults receiving TNF blockers are of concern and deserve further investigation," FDA said. "Long-term studies are necessary to provide definitive answers about whether TNF blockers increase the occurrence of cancers in children because cancers may take a long time to develop and may not be detected in short-term studies."

Last week, FDA also announced that it was adding a boxed warning to the prescribing information of becaplermin (Regranex), a topical cream indicated for the treatment of leg and foot ulcers that are not healing in diabetic patients, about an increased risk of cancer mortality associated with use of three or more tubes of the product.

The warning, FDA explained, is based on the results of two studies that have shown an increased cancer mortality risk among those who have used three or more tubes of becaplermin. In one retrospective study, such use of becaplermin, a recombinant human platelet-derived growth factor, was associated with a five-fold increased risk of cancer mortality.

The studies did not identify any specific cancers for which the product might increase mortality risk. ◆

Notes



Wlodawer Awarded Heyrovsky Medal

Last month, Dr. Alexander Wlodawer, chief of the Macromolecular Crystallography Laboratory in NCI's Center for Cancer Research, received the Jaroslav Heyrovsky Honorary Medal for Merit in Chemical Sciences. The medal, established in 1965, is awarded by the President of the Academy of Sciences of the Czech Republic and recognizes outstanding scientific results in the field of chemistry. Dr. Wlodawer was recognized for his important contribution to the studies of protein structure and also for his advisory role in the revitalization of the Institute of Organic Chemistry and Biochemistry in Prague.

Francis Collins Leaves NHGRI

Dr. Francis Collins recently announced that he will step down as director of the National Human Genome Research Institute (NHGRI) after 15 years leading NIH efforts to map the human genome. Dr. Collins will pursue new professional opportunities and write a book about the use of genetic research to personalize medical prevention and treatment.

NIH Director Dr. Elias Zerhouni referred to Dr. Collins as a "trailblazer in the scientific community." Dr. John Niederhuber, director of NCI, also praised Collins' leadership noting NHGRI's partnership with NCI during the pilot phase of their joint venture, The Cancer Genome Atlas. This landmark project to understand the molecular basis of cancer through genome characterization "is an example of the kind of groundbreaking research two institutes can create, when their focus is on nothing less than the best science for the benefit of patients," Dr. Niederhuber commented. "What Dr. Collins has contributed to these pioneering efforts will one day transform cancer medicine."

Free Telephone Workshop for Cancer Survivors

CancerCare, in collaboration with NCI, the Lance Armstrong Foundation, Intercultural Cancer Council, Living Beyond Breast Cancer, and National Coalition for Cancer Survivorship, will present a teleconference titled "Survivors Too: Family, Friends and Loved Ones" on June 24 from 1:30 to 2:30 p.m. ET.

This is the third of a three-part telephone education workshop series called "The Sixth Annual Cancer Survivorship Series: Living With, Through, and Beyond Cancer."

Part I, "The Importance of Communicating with Your Doctor about Follow-Up Care," took place on April 22, and Part II, "Rediscovering Intimacy in Your Relationships Following Treatment," took place on May 13. Both workshops are archived on the CancerCare Web site.

No phone charges apply. However, pre-registration is required. To access the archive or to register, go to http://www.cancercare.org/TEW. ◆

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"There is no single marker that will be sensitive enough to distinguish all the ovarian cancer patients from healthy women," said Dr. Gil Mor of Yale University, who leads the fourth group. His team has developed panels with two types of markers—proteins produced by ovarian tumors and proteins produced by the body in response to very early changes associated with ovarian cancer.

All of the groups have taken essentially similar strategies, noted Dr. Anna Lokshin at the University of Pittsburgh Cancer Institute, the principal investigator for the fifth study group. "We are all now waiting for the results." The data are being analyzed, and answers could come within months.

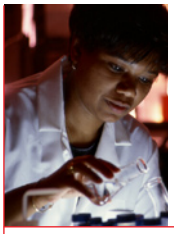
"A lot of people around the country are holding their breath to see the results," said Dr. David Ransohoff, a cancer epidemiologist at the University of North Carolina at Chapel Hill, who consulted on the project.

"These are some of the best groups in the country; they are investigating an important question; and the specimens are among the best available to answer it," he continued. "If the results are positive in these samples, it will be enormously good news for the field." ◆

By Edward R. Winstead

Missed a Highlight?

The *NCI Cancer Bulletin* Archive allows you to search every issue of this online publication since January 2004. That's more than 180 issues' worth of articles on a variety of cancer research topics and updates. ◆



Featured Clinical Trial

Defining Therapy for Recurrent Platinum-sensitive Ovarian Cancer

Name of the Trial

Phase III Randomized Study of Adjuvant Chemotherapy Comprising Carboplatin and Paclitaxel with Versus without Bevacizumab and/or Secondary Cytoreduction Surgery in Patients with Platinum-Sensitive Recurrent Ovarian Epithelial Cancer, Primary Peritoneal Cavity Cancer, or Fallopian Tube Cancer (GOG-0213). See the protocol summary at http://cancer.gov/clinicaltrials/GOG-0213.

Principal Investigators

Dr. Robert Coleman, Dr. Scott Eisenkop, Dr. Deborah Armstrong, Dr. Thomas Herzog, and Dr. Paul Sabbatini, Gynecologic Oncology Group

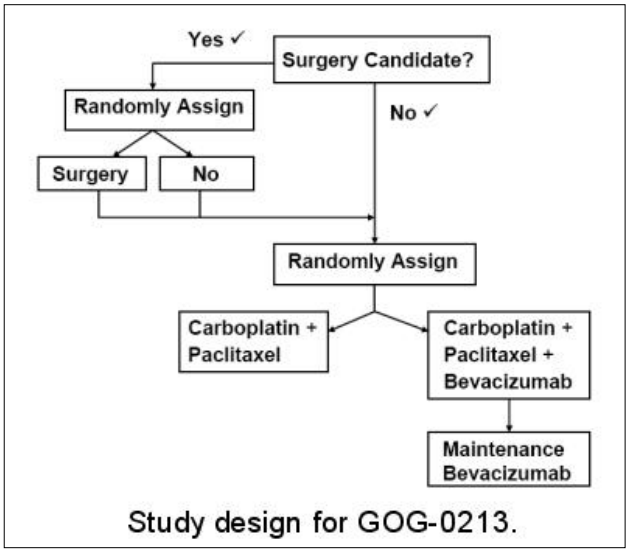
Why This Trial Is Important

Ovarian cancer is one of the most common gynecologic cancers and is expected to strike more than 21,000 U.S. women in 2008. Primary peritoneal cancer and fallopian tube cancer are similar diseases that often respond to the same treatments used for ovarian cancer.

Typically, ovarian cancer is treated with surgery to remove the cancer, followed by combination chemotherapy with a platinum-containing drug (carboplatin or cisplatin) and a taxane, such as paclitaxel. Ovarian cancer that responds to chemotherapy with a platinum-containing drug is called platinum sensitive. Even if it recurs after treatment, platinum-sensitive ovarian cancer may respond again to treatment with a platinum-taxane combination.

Dr. Robert Coleman

While this common therapy does help some women live longer, doctors are eager to find better ways to treat recurrent ovarian cancer. One method under investigation is the addition of the biological agent bevacizumab to combination chemotherapy. Bevacizumab works by blocking the development of new blood vessels to tumors. Another approach, called secondary cytoreductive surgery, is performing another operation to remove the recurrent tumors.



Study design for GOG-0213.

In this phase III clinical trial, women with platinum-sensitive, recurrent ovarian epithelial, fallopian tube, or primary peritoneal cancer will be assessed first to determine whether or not they are candidates for secondary cytoreductive surgery. Surgical candidacy will be determined by whether or not there is a high likelihood of complete tumor removal, based on clinical evaluation and imaging. Women found to be candidates for this surgery will be randomly assigned to undergo it or not. These women will then be randomly assigned to receive combination chemotherapy with carboplatin plus paclitaxel or the same chemotherapy plus bevacizumab, followed by maintenance bevacizumab therapy after the chemotherapy is completed.

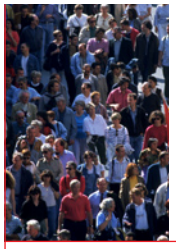
Women who are determined to not be candidates for secondary cytoreductive surgery at the start of the trial will immediately be randomly assigned to receive carboplatin plus paclitaxel chemotherapy or the same chemotherapy plus bevacizumab, which will also be followed by maintenance bevacizumab.

"At this point, the optimal therapy for women with recurrent, platinum-sensitive ovarian cancer is not well defined," said Dr. Coleman. "We have seen positive results from both of these experimental therapies in early stage clinical trials, and with this trial, we are hoping to establish their benefits for women with these cancers."

For More Information

See the lists of entry criteria and trial contact information at http://cancer.gov/clinicaltrials/GOG-0213 or call the NCI's Cancer Information Service at 1-800-4-CANCER (1-800-422-6237). The toll-free call is confidential. ◆

An archive of "Featured Clinical Trial" columns is available at http://cancer.gov/clinicaltrials/ft-all-featured-trials.



Community Update

Cancer.gov En Español Celebrates First Year, Looks Forward to Growth

An announcement last month by the U.S. Census Bureau noted that Hispanics and Latinos are not only the largest minority group in the country, but they are also the fastest growing. In anticipation of their health information needs, NCI launched a Spanish-language Web site, Cancer.gov en español, in April 2007.

"Although Latinos in this country represent a diverse population with respect to cultures, Cancer.gov en español is an important step in the right direction to meet their information needs," says Nelvis Castro, associate director of multicultural and international communications in NCI's Office of Communications and Education (OCE).

The site has had strong reviews, including six NIH Plain Language Awards, an NIH Director's Award, and more than 140 articles publicizing the site across various national Spanish-language markets, including CNN en Español. After it launched, the number of visitors to NCI's Spanish-language Web pages jumped by 10 percent.

"It's not always easy to find relevant and appropriate cancer information in Spanish, but Cancer.gov en español offers this in one easy-to-access Web site," says Dr. Yvette Colón, director of education and internet services at the American Pain Foundation. "We provide several links to it from our Web site, and our Pain Information staff members regularly include it as a resource for callers."

By 2007, many NCI materials were already available in Spanish, notes José Acosta, a technical writer and editor in OCE. "What we needed to develop was a new Web site structure," he says, "one that would be proper for the cultural needs of Latinos."

Among the approximately 46 million Latinos living in the U.S., about half can speak English comfortably. Research shows, however, that Spanish messages have a stronger emotional impact on Latinos than those written or spoken in English. And even among second-generation immigrants, culture influences their preference for images and content that reflect their heritage.

NCI addressed these trends by designing a Web site for Latinos living in the U.S. who are confronting cancer personally, as family members of a cancer patient, or as health professionals seeking cancer research information in Spanish to provide to their patients.

"We're trying to address the myths and beliefs that exist within the Latino community around cancer right from the home page," says Anne Middleswarth, a Web content manager in OCE. Four homepage banners highlight cancer prevention, treatment, detection, and survivorship, and lead to content that corrects misunderstandings about the topics.

"It's become a tool for navigating the health care system," explains Silvia Inéz Salazar, a public health advisor in OCE. She points to the Spanish-language dictionary on the site, which contains more than 5,000 entries and allows people to toggle back and forth between the Spanish and English versions of cancer terms. She notes that both patients and health care providers have used this translation function to improve their communications.

The Web site banner above says, "Facing forward: Life after cancer treatment," to confront the belief that people don't survive cancer.

Members of offices across NCI have helped with content development and promotion of Cancer.gov en español. For example, information specialists at the NCI Cancer Information Service call center in Miami, FL, which answers Spanish-language inquiries from the public, helped test the site before it went live, providing valuable feedback on navigation and the search engine.

The site will continue its expansion in 2008, with targeted development of new pages that reflect the areas of greatest interest and need among Spanish-speaking audiences. ◆

By Brittany Moya del Pino