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THE CLINICAL CANCER LETTER

Cancer research news for clinicians

Oxaliplatin Regimen May Beat Standard For Advanced Colorectal Cancer, NCI Says

Drilling into the NCI clinical trials Web site, visitors may stumble across the following announcement:

"Oxaliplatin Combo May Be Better Treatment for Advanced Colorectal Cancer."

According to the news item, a study led by North Central Cancer Treatment Group found that a regimen containing oxaliplatin slowed the time to progression of advanced colorectal cancer, and produced better survival and toxicity than the current standard of care.

In fact, the NCCTG data and safety monitoring committee

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AACR Annual Meeting:

New Technology May Enable Therapy Tailored To Patient's Predicted Response

SAN FRANCISCO—A new technology developed by government researchers may point the way to a future when cancer treatment is individually tailored on the basis of a "snapshot" that reveals the entire pattern of protein activity in a patient's tumor.

The research was presented this month at the annual meeting of the American Association for Cancer Research.

"Our goal is to improve the effectiveness of cancer treatment by identifying which patients are likely to respond to particular therapy based on individual profiles of protein activity," said Emanuel Petricoin, co-director of the Clinical Proteomics Program, a joint venture of the U.S. Food and Drug Administration and the National Cancer Institute.

Multiple genetic mutations are the underlying cause of most cancers. But the reason these defective genes cause cancer is that they encode abnormal proteins that, either directly or as a result of interaction with other proteins, stimulate or fail to suppress the uncontrolled growth of cancer cells.

"This new technology enables us to look directly at the proteins in the patient's tumor, identify which ones are activated, and observe the effects of treatment on protein interaction," he said. "We can glean this information from a tiny sample of tumor tissue that amounts to about a hundred cells."

Petricoin and his colleagues expect to be able to use this information soon to select the initial therapy most likely to be effective for a patient, monitor the patient's response to therapy, figure out what went wrong if

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Oxaliplatin Data Release Planned For ASCO Meeting

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recommended closing the standard care arm of the study and switched the patients to the oxaliplatin regimen arm.

A new regimen for colorectal cancer that beats the standard of care would appear to deserve more than a subtle statement. Why not a big "rollout" downtown, with HHS Secretary Tommy Thompson opening a press conference with a heartwarming story about his native state?

Instead, on April 24, the news item was tucked into a not-very-noticeable place, on the NCI Clinical Trials Web site: http://www.cancer.gov/clinical_trials.

Releasing information from important clinical trials is rarely a straightforward and orderly process. In this case, NCI officials said they felt an obligation to inform the public about the findings, and American Society of Clinical Oncology officials said they wanted to allow time for reasonable peer review.

Also, reports of significant findings and their review are among top reasons for 25,000 people to attend the upcoming ASCO annual meeting in Orlando. The oxaliplatin data are under an embargo until their presentation on May 18.

"From our point of view, the process of releasing important trial results in a 'rolling' fashion has worked well in this case, and may be useful in other situations when a result emerges suddenly," said Richard Kaplan, chief of the NCI Clinical Investigations Branch.

"The ease and transparency of communication via the Web allows the outcome to be known right away, and then additional detail and perspective are progressively made available as soon as they are ready," Kaplan said. "NCI can ask everyone to 'watch this space' to get a full picture of the importance of the trial results. Meanwhile, those who have the most urgent need for information, study subjects and other patients and oncologists, can be informed of the direction of the trial outcome; they need not wait until a clean dataset is ready, or until opinion leaders have been able to view the data and put it into clear clinical perspective."

ASCO would have preferred to limit the release of information to trial participants and investigators, said Charles Balch, the society's executive vice president and CEO.

"The NCI and the investigators felt an obligation, which I think is correct, to inform the patients on the trial and the investigators," Balch said. "However, we were disappointed that they chose to put what they did on the public Web page."

Oxaliplatin, a drug sponsored by Paris-based Sanofi-Synthelabo, is not approved in the U.S., which makes the release of information less urgent, Balch said. "The drug is not available outside a clinical trial, so it's not a public health issue," he said.

At ASCO, the results of the trial, N9741, will be presented by investigators from NCCTG and critiqued by Leonard Saltz, the gastrointestinal oncologist whose regimen of CPT-11, 5-fluorouracil and leucovorin now appears to be inferior to oxaliplatin, 5-FU and LV.

"There will be discussion and debate about the context of this drug relative to other drugs, such as CPT-11, and that's part of discussion among peers that will occur at the ASCO meeting," Balch said. "Experts need to debate this."

Kaplan agreed that it would be premature to release data at this point.

"The impact of the N9741 results, like those of any trial, needs to be considered carefully not only within the context of the trial itself, but also in relation to data from other studies, the impact of second-line regimens, and the full scope of therapeutic options," he said.

"The data that led to the DSMB decision to unblind the results were from an interim (albeit

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planned) analysis at a point where a good deal of additional data were still rolling in quite quickly," Kaplan said. "A brief delay before ASCO allowed NCCTG to carry out what is always a critical step in preparing any trial for presentation—calling in outstanding data, performing quality checks, and locking the dataset."

Watch This Space

The NCI statement contained no data:

"Patients with newly diagnosed advanced colorectal cancer who received a multidrug regimen containing the investigational agent oxaliplatin appear to have fared significantly better than patients who received the current standard treatment, according to preliminary data from a randomized, phase III clinical trial sponsored by NCI.

"The preliminary analysis showed that patients receiving the regimen known as FOLFOX (oxaliplatin, together with infusional 5-FU and LV) had a significantly longer time to disease progression, significantly better overall survival, a significantly higher response rate, and lower toxicity than patients receiving a regimen known as IFL (CPT-11, together with bolus 5-FU and LV). IFL (also known as the Saltz regimen) has been the standard treatment for advanced colorectal cancer since April 2000.

"The data, although preliminary, appear to show a very strong trend in favor of the FOLFOX regimen. The trial, known as N9741, is coordinated by the North Central Cancer Treatment Group in collaboration with four other cancer research cooperative groups in the U.S. and Canada.

"The current analysis involves 795 patients with previously untreated metastatic colorectal cancer who enrolled in the study between March 1999 and April 2001.

"During a planned interim analysis of the trial last week, the independent monitoring committee charged with oversight of the trial reviewed the results to date and found the FOLFOX data promising enough to warrant significant changes to the trial.

"Consequently, enrollment onto the IFL arm of the trial has been discontinued. New patients will continue to be enrolled on the FOLFOX arm pending other arrangements for access to oxaliplatin. Patients on the other arms of the trial who at any point are not responding to their current treatment will be permitted to switch to the FOLFOX regimen. (In the non-FOLFOX arms of the trial, patients receive either IFL or a combined regimen consisting of [CPT-11] and oxaliplatin only. It's still too early to draw any conclusions about the effectiveness of the latter regimen compared with that of FOLFOX.).

" 'Patients and their doctors are being advised of these findings as quickly as possible,' said Richard Kaplan, of the NCI Cancer Treatment and Evaluation Program. 'Even though the data are preliminary and stem from a single randomized trial, the data monitoring committee felt that the apparent superiority of FOLFOX should be made known to patients and clinicians.

"Collection of all the trial data is now under way. Details concerning the magnitude of the differences between the two regimens are expected to be announced within the next few weeks. Meanwhile, discussions are under way between NCI and the maker of oxaliplatin, the French pharmaceutical company Sanofi-Synthelabo, to permit more patients with metastatic colorectal cancer to receive treatment with the investigational drug, which is currently not licensed for use in the U.S."

Two- To Three-Month Survival Advantage?

Sources said the data and safety monitoring committee overseeing the trial determined on April 10 that the oxaliplatin-containing regimen had surpassed the CPT-11-containing regimen.

With the data absent, colorectal cancer experts appear to be enjoying the guesswork.

"I can guess what the data shows, because the study was terminated abruptly," ventured one expert who performed this exercise on condition that his name would not be used. "It didn't terminate because of bad news. One arm had to have been doing better, and it wouldn't have closed for anything but survival, so one arm had to have had a survival advantage, and my guess it's the oxali arm. Otherwise, there wouldn't be so much excitement."

According to the protocol, in order to close an arm in the trial, the planned interim analysis had to find superiority in time to tumor progression with the p-value of less than .0005. Finding a survival advantage in a smaller study powered to detect time to progression means the survival advantage is substantial.

"It would have to be in the range of two to three months," the expert said.

The NCCTG trial is being rewritten to remain open, to serve as an expanded access program, sources said.

"This is a drug that may become available for

use without any data available, outside an ASCO presentation," said an expert familiar with development of oxaliplatin.

The Eternal Question: Bolus Vs. Infusion 5-FU

Though N9741 shows a survival advantage for the oxaliplatin regimen, the trial's implications for the approval of oxaliplatin by FDA aren't clear cut:

—The trial was launched two years ago to compare progression-free survival in six treatments of colorectal cancer, rather than to provide a basis for approval of any drug or regimen. Ultimately, three of the trial's arms were dropped. One arm, 5-FU/LV, was dropped after it was surpassed by the Saltz regimen as the standard of care, and two other regimens were dropped because of toxicity problems.

—The trial compares regimens, not single drugs. FDA has required data on the contribution of all drugs contained in multidrug regimens.

—The trial isn't even in the same indication as the registration trials sponsored by Sanofi. While N9741 is conducted in the first-line setting, Sanofi is testing oxaliplatin as a second-line treatment.

—The oxaliplatin and CPT-11 regimens aren't using the same methods of administering 5-FU/LV. The oxaliplatin regimen uses infusion. The CPT-11 regimen uses bolus.

This distinction in the administration of 5-FU/LV may be significant, experts say.

"[Aimery] deGramont has previously published a randomized trial showing that infusional 5-FU produces significantly better time to progression and less toxicity than daily 5-FU/LV a-la-Mayo," said Richard Schilsky, associate dean for clinical research at the University of Chicago. "So, the infusional 5-FU could be an important contributor. Therefore, it would be nice to know how FOLFOX compares to [the Douillard regimen] CPT-11 and infusional 5-FU."

Schilsky said he has not seen the data from N9741.

—Selection of patients can be significant, too. For example, an imbalance in the number of patients with the performance status of ECOG 2, who generally don't benefit from treatment, can alter the result in either arm.

Approval for First and Second Line?

The full spectrum of news about oxaliplatin is appears to be broader than ASCO presentations reflect.

On April 29, five days after the NCI announcement of the NCCTG findings, a press release from Sanofi reported that FDA has granted fast-track review for the application for oxaliplatin as a second-line therapy for advanced colorectal cancer.

The company study (EFC 4584) tested the drug in patients whose disease progressed on the Saltz regimen or within six months after treatment.

The fast track designation doesn't amount to an inside track at FDA. It means that the drug has the potential to address an unmet medical need, that the sponsor would be allowed to submit the New Drug Application in parts, as a "rolling NDA," and that FDA would have to complete review of the application on an accelerated schedule, within six months.

"We are working very closely with the independent data and safety monitoring board for this trial to determine appropriate handling of data from a planned interim analysis of objective response rate, time to tumor progression, and reduction in tumor-related symptoms," said Mace Rothenberg, Ingram associate professor of cancer research at Vanderbilt University and the principal investigator on EFC 4584.

The best-case scenario for Sanofi may be that data from the NCCTG trial in the first-line indication and emerging data in the company-sponsored trials in the second-line indication, as well as pooled data accumulated in countries where oxaliplatin is approved, would support an across-the-board approval for oxaliplatin in advanced colorectal cancer.

"Ideally, these trials will provide complementary data addressing the role of oxaliplatin in first and second line, not necessarily limiting labeling to one setting or another," Rothenberg said. "One can say, let's not view this in isolation, but rather in the context of many completed and published phase III trials. The level of comfort regarding activity, toxicity, and tolerability may actually be greater because of these other trials."

This will be the second time oxaliplatin has been reviewed by FDA. In March 2000, the agency's Oncologic Drugs Advisory Committee recommended against approval of the drug. At that time, Sanofi and U.S. partner Eli Lilly & Co. sought approval based on European studies powered for response rate and progression-free survival. The company's survival assessment involved extensive statistical analysis that went beyond the simple log rank test (**The Cancer Letter**, March 24, 2000).

Soon after ODAC nixed the drug, Eli Lilly dropped out of the U.S. development program, and oxaliplatin reverted to Sanofi.

Low-Dose Aspirin Cuts Risk Of Colorectal Growths

SAN FRANCISCO—Three studies presented at the annual meeting of the American Association for Cancer Research describe a range of findings for two common products, aspirin and green tea, for prevention or treatment of cancers of the large bowel, esophagus, stomach, and prostate.

Low-dose Aspirin Reduces Risk of Recurrent Colorectal Growths Linked to Cancer

A large, prospective study of two different doses of aspirin to prevent recurrence of colorectal adenomas found modest preventive benefit with both regimens, but the lower dose was associated with a higher reduction in risk. Adenomas are benign epithelial tumors that may progress to invasive cancer.

"This is the first clinical trial focused on the protective effects of aspirin against the development of tumors in the large bowel," said John Baron, professor of medicine at Dartmouth Medical School in Lebanon, NH. "We were surprised to find that the lower dose showed more effect."

Compared with the placebo group, patients taking 80 mg per day (one baby aspirin) reduced their risk of recurrent adenomas by 19%; those taking 325 mg (one standard aspirin) had a 4% reduction in risk.

When the data were analyzed according to the more aggressive types of adenomas (tubulovillous or villous) that were initially removed, risk reductions were 40% with the low-dose regimen and 19% with the high dose.

Patients were eligible for the study if they had at least one adenoma removed within the three months preceding the study, had no known cardiovascular disease or other conditions usually treated with aspirin (e.g., long-standing arthritis, headaches), and had no hereditary cancer syndromes. Potential study participants took 325 mg of aspirin daily for three months to identify anyone who had problems with the highest protocol ose or with compliance. Afterward, 1,121 patients were randomly assigned to one of three groups: placebo, 80 mg of aspirin per day, or 325 mg of aspirin per day for an average length of 34 months.

"These two doses were tested because they reflect amounts often used for heart disease prevention, and we wanted to be consistent in our study to avoid the possibility of conflicting recommendations for these two health issues at a future date," said Baron.

The Dartmouth investigators will continue to follow these patients in an observational study design to track aspirin use, which is now optional for all three study groups, and to monitor for recurrent adenomas and development of colorectal cancer.

Green Tea Shows Protective Effect Against Gastric and Esophageal Cancers

The first biomarker-based prospective study of green tea and cancers of the stomach and esophagus demonstrates a strong protective effect: subjects demonstrating the presence of tea polyphenols in their single-void urine specimens exhibit a lower risk for both cancers. The new data, presented here, confirm reports from earlier retrospective research.

Tea polyphenols are antioxidants that have been shown to have chemoprotective benefits for cancers at these and other sites.

"We found approximately a 50% reduction in relative risk, which is confined to subjects with low serum levels of carotene, which is also an antioxidant," said Can-Lan Sun, lead author of the study report, and a researcher in the Department of Preventive Medicine at University of Southern California Norris Comprehensive Cancer Center in Los Angeles. "It appears that tea polyphenols may play an important protective role in people who have low levels of other antioxidants."

Investigators at USC collaborated with the Shanghai Cancer Institute on a prospective cohort study involving 18,244 middle aged or older men in Shanghai, China. Chinese men have a much higher risk for gastric and esophageal cancers than the U.S. population, but prognoses of these cancers are universally poor. The overall five-year survival rate for gastric cancer is about 21%; under 10% of patients with esophageal cancer live more than 12 months after diagnosis.

In this study, levels of two tea polyphenol markers, epigallocatechin (EGC) and epicatechin (EC), were measured in urine samples taken from 190 men with gastric cancer and 42 men with esophageal cancer before their malignancies were diagnosed. These data were compared with urinary EGC and EC levels for 772 control subjects from the

same cohort, matched for age and other relevant factors to the cancer cases. The investigators found a statistically significant association between presence of EGC in baseline urine and reduced risk of gastric and esophageal cancer among cohort subjects. No such association was observed for EC.

Green Tea Therapy Not Effective In Advanced Prostate Cancer

A phase II study of green tea as treatment for advanced prostate cancer demonstrated disappointing results, according to researchers at the Mayo Clinic and the North Central Cancer Treatment Group who reported their data here.

Only one patient of 42 had a 50% drop from baseline measurements of prostate-specific antigen (PSA) and the response was brief.

"In this preliminary investigation, we tested high doses of green tea, but we did not see the favorable effects for which we had hoped," said Aminah Jatoi, lead investigator and assistant professor in Mayo's Department of Oncology, Rochester, MN.

The protocol consisted of six one-gram doses per day of highly concentrated, presweetened green tea specially formulated for this study. Patients were allowed to take the tea as they wished: hot, iced, in juice, diluted, or with additional sweetener. After roughly one month of treatment, which had been planned to be administered for at least four months, dropout rates were high because of disease progression and side effects attributed to the highly concentrated green tea preparation.

In laboratory studies, the polyphenols in green tea have been shown to impede the growth of prostate tumors that don't depend on steroid hormones called androgens. The research team hoped that green tea would demonstrate a similar effect in a group of patients with androgen-independent cancer that had spread outside the prostate and had failed to respond to other therapies.

The Mayo Clinic/NCCTG investigators considered using decaffeinated tea, but because other investigators had suggested that decaffeination may also remove anticancer substances from the tea, they opted not to. However, some of the side effects observed in this study may have been related to the caffeine content of this high-dose green tea preparation.

"Although these findings are not encouraging for green tea for this type of prostate cancer, I think we send a very important message to people with cancer," said Jatoi. "Oncologists, researchers, and others are examining unconventional approaches and are receptive to the possibility that such therapies may help."

Clinical Proteomics Program Analyzes Patient "Profiles"

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the cancer recurs, and choose another therapy or combination of therapies that targets the abnormal protein pathway responsible for the recurrence. The researchers are currently testing the technology with several clinical collaborators in patients with breast and ovarian cancer who are taking part in a clinical trial at the National Institutes of Health.

In collaboration with the NCI, the Clinical Proteomics Program is analyzing patients treated with the drug trastuzumab (Herceptin), followed a month later by the drug paclitaxel (Taxol). After analyzing the protein "profiles" of about 20 patients to date, the investigators noted a distinct difference in patients who respond to the therapy and those who don't.

In responders, trastuzumab seems to reduce activation of a protein called Akt, which is involved in sending signals that suppress apoptosis in cancer cells, or programmed cell death. In non-responders, however, trastuzumab was found to have no effect on Akt.

"We think that in the responders, Herceptin is reducing activation of Akt, which destroys the signaling pathway that tells cancer cells to survive," said Petricoin. "When the patients receive Taxol, that drug throws the cells into apoptosis. But in the non-responders, the pro-survival signals remain intact and the cancer cells refuse to die even when Taxol is given."

The new protein analysis technology brings together two technological advances. The first, known as Laser Capture Microdissection, enables the rapid dissection of cancer cells directly from a patient's tumor specimen. The second, known as a protein reverse phase lysate microarray, makes it possible to analyze a thousand proteins on a single laboratory slide.

Petricoin and his colleagues are continuing to test the technology in more patients in the breast and ovarian cancer trial as well as in other trials that are just now beginning accrual to evaluate new molecularly targeted drugs such as STI571 (Gleevec) and ZD1839 (Iressa).

Predict Early Response to Chemotherapy

In another study presented at AACR, a novel diagnostic test may be able to predict after a single dose of chemotherapy whether an individual cancer patient is likely to respond to the treatment, researchers reported here.

"We think this technology will enable clinicians to make better treatment decisions for individual patients by monitoring response to therapy with greater sensitivity and speed," said Neil Steinmetz, vice president and medical director of the Theseus Imaging division of North American Scientific, Inc., which developed the technology, a radiopharmaceutical known as Apomate.

Currently, a patient usually undergoes four or five courses of chemotherapy, with all the attendant side effects, before doctors can tell whether treatment is going to be effective. By that time, the toxic drugs may have killed so many normal cells or the tumor may have continued to grow so that it may be too late to switch the patient to another chemotherapy regimen, Steinmetz said.

Apomate works by measuring changes that occur on the outer membrane of cancer cells early in the cell death process. The test is conducted before chemotherapy begins to measure the natural level of cell death occurring in the cancer cells. Another test is done one to three days after the first dose of chemotherapy, and results are compared to the baseline test.

"If a higher level of cell death is observed after the first dose of chemotherapy, that provides initial evidence the tumor is responding to treatment," said Steinmetz. "However, if there is no increase in cell death seen after the first dose of chemotherapy, the data suggests that the patient is unlikely to benefit from additional doses of the same treatment."

Initial results from an international clinical trial designed to test the safety of Apomate are encouraging, Steinmetz said. All seven patients with advanced lymphoma, lung cancer, or breast cancer who had a positive result on Apomate responded to treatment either partially or completely.

Alternately, six of eight patients with a negative result on Apomate failed to respond to chemotherapy and developed progressive disease or died. The Apomate test takes advantage of the fact that, early in the process of apoptosis, or programmed cell death, a component of the membrane of tumor cells called phosphatidylserine (PS) migrates to the membrane's outer surface. Apomate combines a natural human protein called annexin V, which attaches to PS, with a radioactive tracer called technetium, which releases a signal that can be detected outside the body by a special camera. These signals are used to measure the level of cell death within the tumor. Technetium is widely used as a tracer in medical imaging tests and has the advantages of disappearing from the body within about a day. An Apomate test exposes the body to about the same amount of radiation as a computed tomography (CT) scan of the abdomen, said Steinmetz.

New Treatment Approach To Treating Brain Tumor

SAN FRANCISCO—A new approach to treating a highly lethal brain tumor extended patients' survival by an average of seven months, according to scientists presenting data from a preliminary trial here.

The treatment strategy involved inducing hypothyroidism in patients with recurrent gliomas, followed by treatment with tamoxifen.

"We concluded that hypothyroidism enhanced the effect of tamoxifen, but cannot exclude that there may also be a direct beneficial effect of hypothyroidism on extending survival in cancer patients," said Aleck Hercbergs, a radiation oncologist at the Cleveland Clinic Cancer Center in Cleveland, Ohio, who led the group that conducted the study. "This offers further evidence for the idea that the thyroid gland is an important internal modulator of cancer."

The trial involved 38 patients with recurrent glioma, an aggressive brain tumor that is generally unresponsive to conventional chemotherapy or radiation. Half of the patients given the experimental treatment regimen became hypothyroid and survived for an average of 11 months, compared with four months for the patients who did not become hypothyroid.

Three of the patients who became hypothyroid survived for more than two years, whereas the longest surviving patient in the group who did not become hypothyroid lived for eight months. Only one patient experienced symptoms possibly attributable to hypothyroidism.

"We expected only about a quarter of the patients with induced hypothyroidism to respond to the tamoxifen since only about 25% of gliomas overproduce PKC-a," said Hercbergs. "These results

certainly add to a growing body of evidence that suppressing thyroid function alone may improve response to cancer treatment."

Hercbergs and his colleagues are now testing the same treatment approach in patients with newly diagnosed glioma.

Experimental Drug For Melanoma

An experimental drug originally developed to treat high cholesterol is showing promise as both a treatment and a preventive agent for a lethal form of skin cancer, researchers report here.

"Three of nine patients with metastatic melanoma who were treated in an initial clinical trial responded well to the drug, one of whom has remained on the treatment for three years," said Marianne Powell, senior research scientist at Stanford University School of Medicine in California.

All of the patients had disease that had not responded to previous surgery and chemotherapy. An unusual feature of the drug, known as SR45023A (Apominetm), is that it appears to be effective both taken orally and applied to the skin, Powell said.

Patients in the clinical trial took the experimental drug by mouth. In the future, said Powell, it could become an ingredient of sunscreen and sunblock lotions to protect against melanoma.

Two more clinical trials are underway, one to test the efficacy of single agent SR45023A against recurring melanoma, and another in the treatment of metastatic breast cancer.

Phenoxodiol Slows Cancer Progression

Preliminary clinical trial results of the novel anti-cancer drug phenoxodiol indicate that it slowed cancer progression in six out of 10 patients at doses that were well tolerated.

The interim trial results were presented at the annual meeting of the American Association for Cancer Research by researchers from the Cleveland Clinic's Taussig Cancer Center.

Phenoxodiol represents a new direction for anti-cancer therapy. The drug targets the underlying control mechanism in cells that determines whether a cell will survive or die. This mechanism malfunctions in cancer cells, preventing them from dying or being killed by drugs. Phenoxodiol targets the activities of key members of this control mechanism including sphingosine kinase and the caspase proteins. Phenoxodiol is being developed by Marshall Edwards Inc.

Patients on the trial have a variety of cancers that failed to respond to standard therapy, including colon cancer, melanoma, thymic cancer, prostate cancer, RCC and TCC.

In the trial, phenoxodiol is administered by intravenous infusion for six weeks in the first instance. Treatment can be continued past six weeks if there is no evidence of tumor progression or serious toxicity. Six of 10 patients remained on phenoxodiol beyond six weeks following evidence of stabilization.

NCI-Approved Clinical Trials

The National Cancer Institute's Cancer Therapy Evaluation Program Approved the following clinical research studies last month. For further information about a study, contact the principal investigator listed.

Phase I

Phase I Study of G3139 in Combination with Cytarabine and Daunorubicin in Previously Untreated Patients with Acute Myeloid Leukemia >= 60 Years of Age. Ohio State University Hospital, protocol 4630, Marcucci, Guido, phone 614-293-8723.

Phase II

Phase II, Open-Label, Randomized Trial of Zoledronic Acid (Zometa Ô) versus Zoledronic Acid and BMS-275291 in patients with Hormone Refractory Prostate Cancer. Mayo Clinic, protocol 5361. Pili, Roberto, phone 410-502-7482.

Phase II Study of Rituximab and Short Duration, High Intensity Chemotherapy with G-CSF Support in Previously Untreated Patients with Burkitt Leukemia/Lymphoma (Acute Lymphoblastic Leukemia-[L3] and Small Non-Cleaved Non-Hodgkin's Lymphoma. Cancer and Leukemia Group B, protocol CALGB-10002, Byrd, John, phone 614-293-7509.

Phase II Study of Oral EGFR Tyrosine Kinase Inhibitor OSI-774 in Patients with Malignant Pleural Mesothelioma. Southwest Oncology Group, protocol S0218, Garland, Linda, phone 520-626-3434.

Phase III

Randomized Phase III Trial Comparing Immediate Versus Deferred Chemotherapy After Radical Cystectomy in Patients with pT3-pT4, and/or N+M0 Transitional Cell Carcinoma of the Bladder. Southwest Oncology Group, protocol EORTC-30994, Benson, Mitchell, phone 212-305-5201.