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THE CLINICAL CANCER LETTER

Cancer research news for clinicians

Advanced Ovarian Cancer Responds To Irofulven In Phase II Studies

Irofulven, a new anticancer compound, produced objective tumor responses in patients with advanced ovarian cancer in two phase II studies, according to presentations at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics held in Miami Beach, Fl., this month.

Results were reported for 68 patients with refractory or recurrent disease following platinum and/or paclitaxel treatments. Of the 55 patients evaluable for efficacy, 10 patients demonstrated objective responses; one patient had a complete clinical response and nine patients had partial

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Clinical Trials:

Older Colon Cancer Patients Also Benefit From Chemotherapy, NCCTG Study Finds

Older patients diagnosed with mid-stage colon cancer benefit as much from chemotherapy after surgery as younger patients with the disease, according to a study led by the North Central Cancer Treatment Group, a clinical trials cooperative group based at Mayo Clinic in Rochester, Minn.

The study results, published in the Oct. 11 issue of New England Journal of Medicine, conclude that age alone should not determine whether an older patient is offered chemotherapy after surgery for treatment of stage II and III colon cancer.

Daniel Sargent, a Mayo Clinic statistician and lead researcher on the study, analyzed the medical records of 3,351 patients diagnosed with colon cancer. These patients had previously participated in seven different randomized clinical trials conducted around the world to test the effectiveness of 5-FU based surgical adjuvant chemotherapy for colon cancer.

"We found that patients age 70 and older, who were judged by their physicians to be fit enough to undergo chemotherapy, had the resiliency to successfully withstand the side effects," said Sargent. "Most importantly, the older patients benefited as much from the chemotherapy as younger patients."

The study showed that chemotherapy reduced the risk of death after surgery for colon cancer by 24 percent. The overall five-year survival rate for patients who had chemotherapy after surgery was 71 percent, compared with 64 percent for patients who did not receive chemotherapy.

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Irofulven Produced Response In Advanced Ovarian Cancer

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responses.

Patients with partial responses remained progression free for more than three and up to 20 months. In addition, 17 patients had stable disease and remained progression free for one to nine months. Irofulven was administered for four or five consecutive days every 28 days.

The studies were conducted by the drug sponsor, MGI Pharma Inc., and the U.S. National Cancer Institute. The NCI-sponsored trial data included one complete response, six partial responses, and 13 patients with stable disease. The MGI-sponsored trial data included three partial responses and four patients with stable disease.

At the meeting, sponsored by the American Association for Cancer Research, NCI, and the European Organization for the Research and Treatment of Cancer, 10 posters were presented on irofulven's antitumor activity and mechanism of action in a variety of cancers.

"These results further highlight irofulven's unique antitumor activity either alone or in combination with other agents, and validates our continuing efforts to develop the drug to treat a wide variety of human cancers," said John MacDonald, senior vice president of R&D at MGI.

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Three presentations included updated results from a phase I trial that evaluated the side effects, antitumor activity and pharmacokinetics of irofulven when administered using weekly dosing schedules. Data from this trial demonstrate that irofulven produced significant antitumor responses, including a complete tumor response in an ovarian cancer patient, with a much better tolerance profile than with the previous dosing schedules of four or five consecutive days every 28 days.

"The data from the weekly dosing phase I trial is relevant because it confirms that irofulven continues to be active when given on a more tolerable dosing schedule," said Eddie Reed, director at the Mary Babb Randolph Cancer Center, University of West Virginia, and an NCI trial investigator. "In particular, the every-other-week dosing schedule is recommended for ongoing and future trials based upon an improved tolerance profile and an ability to deliver comparable overall dose intensity to patients. We are clearly seeing progress. Further studies of irofulven in a variety of tumor types, including ovarian cancer, are definitely warranted using the intermittent weekly dosing schedule."

Another poster presentation highlighted the clinical safety and efficacy of irofulven when administered to patients in combination with Camptosar (CPT-11 or irinotecan). Objective responses and tumor marker responses were observed in patients with non-small cell lung and colorectal cancers. The most common side effect observed with every-other-week administration of both agents was decreased white blood cell counts.

Portions of the phase I data on irofulven when administered on weekly dosing schedules were also presented at the European Conference on Clinical Oncology held in Lisbon, Portugal.

Irofulven (also known as MGI 114, hydroxymethylacylfulvene, or HMAF) is the first product candidate being developed by MGI Pharma from its family of proprietary anti-cancer compounds called acylfulvenes. Irofulven is currently being tested in a series of clinical trials for the treatment of solid tumors, across a variety of cancers. Irofulven has demonstrated promising antitumor activity as a single agent in clinical testing against pancreatic, ovarian, and prostate cancers. Last February, MGI began a pivotal phase III trial of irofulven in advanced-stage, gemcitabine-refractory pancreatic cancer patients. Irofulven is also being studied for use in combination with Camptosar, Gemzar (gemcitabine hydrochloride),

and Taxotere (docetaxel).

Side effects from irofulven are similar to marketed chemotherapies and include bone marrow suppression (decreases in platelets or white blood cell counts), nausea, vomiting, fatigue, and visual disturbances.

* * *

MG98, a second-generation antisense oligonucleotide, was well tolerated with an improved side effect profile when compared to first-generation antisense oligonucleotides, in patients with advanced solid tumors, according to data from a phase I study presented at the conference.

MG98 targets mRNA for the nuclear enzyme DNA methyltransferase, which is responsible for silencing tumor suppressor genes. MGI and MethylGene are developing MG98 for the purpose of blocking production of DNA methyltransferase. Preventing DNA methyltransferase production may allow tumor suppressor genes that have been silenced by hypermethylation to be re-activated. MG98 is well tolerated and has already demonstrated anti-cancer activity in Phase 1 trials.

In the phase I study, clear evidence of MG98 antitumor activity was observed in a patient with previously treated renal cell carcinoma that displayed an objective, partial tumor response of approximately 75 percent that was maintained for approximately one year on treatment. In addition, further evidence of MG98 antitumor activity was observed in two mesothelioma patients who displayed stable disease with durations of six and 14 months, respectively, while receiving MG98 treatment.

"The role of DNA methylation in the causation and progression of human cancer is an area of very active recent research," said Michael Cullen, vice president of clinical affairs and chief medical officer at MGI. "Our research with our partner MethylGene on MG98 has demonstrated that selective inhibition of DNA methyltransferase results in tumor growth inhibition or tumor regression. Targeting the re-expression of silenced tumor suppressor genes at the molecular level is considered one of the most exciting new approaches for cancer therapeutics today."

One preclinical presentation reported the ability of MG98 to specifically inhibit the enzyme DNA methyltransferase-1, resulting in the re-expression of methylation-silenced tumor suppressor genes and causing inhibition of human tumor cell growth in both cell culture and animal models. A companion presentation highlighted the ability of combined administration of MG98 and 5-aza-deoxycytidine to produce synergistic reactivation of tumor suppressor genes as well as synergistic inhibition of human tumor cell growth in culture and in animal models. A fourth presentation reported a preclinical safety profile of MG98 in non-human primates that was very well tolerated.

MGI and MethylGene began a phase II trial of MG98 in head and neck cancer patients in November 2000, and began a phase II trial of MG98 in renal cell carcinoma (kidney cancer) in August 2001. MGI and MethylGene intend to further evaluate MG98 in other cancers where silencing of tumor suppressor genes by DNA methyltransferase has been documented.

Along with MG98, MGI licensed a complementary small molecule inhibitor of DNA methyltransferase program that shares the same goal of preventing methylation and silencing tumor suppressor genes. The small molecules are being designed and screened for their potential to bind to DNA methyltransferase and block its activity, rather than prevent its production.

As part of MGI's agreement with its partner MethylGene Inc., MGI has the exclusive license to develop, market and sell in North America MG98 and any small molecule inhibitor of DNA methyltransferase derived from the two companies' cancer research collaborations.

Clinical Trials:

Older Colon Cancer Patients Benefit From Chemotherapy

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People age 70 years and older comprise more than 50 percent of patients with colon cancer.

According to Richard Goldberg, a Mayo Clinic oncologist and co-researcher on the study, chemotherapy treatment after surgery is known to significantly improve the survival rate of patients with stage III colon cancer and may benefit some patients with stage II colon cancer. These cancers are considered mid-stage and potentially curable.

However, he said, questions often arise whether elderly patients can physically withstand chemotherapy treatments.

New or existing medical problems are more common in older patients and may interfere with the ability of elderly patients to tolerate the side effects of chemotherapy.

This study dispels some of those concerns.

"The results of our study should reduce concerns about excess toxicity and reassure physicians and patients that selected patients over the age of 70 can tolerate and benefit from chemotherapy as much as younger patients," said Goldberg.

Rare Lung Disease Raises Risk Of Meningiomas

Scientists at the National Heart, Lung, and Blood Institute of the National Institutes of Health found that women with a rare lung disease known as LAM (lymphangioleiomyomatosis) have a high prevalence of meningiomas, a type of brain tumor.

The study, published in the October 17 issue of the Journal of the American Medical Association, is the first to document the extent of the association between LAM and meningiomas.

"These findings provide important new information on the nature of this disease and have implications for both the diagnosis and treatment of patients with LAM," said NHLBI Director Claude Lenfant.

The meningiomas were detected in an ongoing study of the natural history of LAM. LAM is associated with a rare genetic neurological disorder called tuberous sclerosis.

In an effort to determine whether patients with LAM also showed signs of tuberous sclerosis, NHLBI scientists performed magnetic resonance imaging and computed tomography brain scans on 250 women with the lung disease. They were looking for brain abnormalities called "tubers," one of the criteria for diagnosing TS. Unexpectedly, MRI scans revealed that 8 patients had meningiomas, a rate that far exceeds the 1 in 20,000 expected in the general population.

According to the investigators, it is not clear whether the meningiomas are caused by LAM itself, hormonal treatments for the disease, or a combination of the two. They note that the abnormal smooth muscle cells found in the lungs and other tissues of LAM patients produce certain growth factors that are believed to foster meningiomas. However, the possibility that the meningiomas have a hormonal cause has implications for the overall treatment of LAM.

Because LAM occurs primarily in women of childbearing age, it has been thought to be affected by hormonal factors. As a result, it has been commonly treated with the hormone progesterone.

However, studies have found that progesterone can stimulate growth of meningiomas. Anti-progestins have even been used to treat meningiomas.

"We cannot rule out the possibility that the high prevalence of meningiomas may be a result of both LAM and progesterone therapy," said Joel Moss, chief of NHLBI's Pulmonary-Critical Care Medicine Branch and lead investigator of the study, which was conducted at the NIH Clinical Center in Bethesda, MD.

Moss noted that although some of the women in the study had never been exposed to progesterone, low doses in contraceptives or hormone replacement therapy could have played a role in initiating the tumor or fueling its growth.

Moss and colleagues recommend using MRI to screen for meningiomas in LAM patients and if the tumors are found, they advise against the use of progesterone. The scientists also suggest that patients with meningiomas have yearly MRI scans to evaluate tumor growth. Surgery is the preferred treatment for these tumors which are slow-growing and rarely spread to other parts of the body.

An estimated 8,000 U.S. women have LAM, which is characterized by an unusual type of muscle cell that invades and obstructs the tissue of the lungs, including the airways, and blood and lymph vessels. Over time, these muscle cells interfere with the lung's ability to supply oxygen to the rest of the body. The progression of the disease varies among patients, as does survival, which may extend more than 20 years after diagnosis.

According to Moss, patients with LAM are often misdiagnosed, partly because many of the early symptoms are similar to other lung diseases. "A common symptom of LAM is shortness of breath, which is seen in other lung diseases such as asthma and emphysema," he said. "Other symptoms of LAM include chest pain and coughing up blood-stained sputum or blood."

Moss noted that both spontaneous and inherited forms of LAM have been reported. LAM's connection to tuberous sclerosis has been documented and there is evidence that both diseases can have a common genetic basis.

To increase understanding about the clinical course of LAM, including its connection to tuberous sclerosis, Moss and colleagues at NHLBI are conducting research as part of an Institute-funded study of patients with LAM. Moss is seeking patients with LAM, including those who may have been

diagnosed with TS.

For further information on LAM studies conducted at NIH: http://clinicalstudies.info.nih.gov/. Information on the disease can be found at http://www.nhlbi.nih.gov.

Study Tracks Lifestyle Factors For Cancer Burden In Blacks

The National Cancer Institute has awarded a multi-million-dollar grant for a potentially landmark study to determine why African Americans are more likely than other groups to develop cancer and to die from the disease.

The grant will provide an anticipated $22 million over five years to fund the "Southern Community Cohort Study," which will enroll and follow 105,000 people—two-thirds of them African-Americans—in six southeastern states. The group, or cohort, will be tracked to identify genetic, environmental and lifestyle factors that contribute to cancer development.

It will be the first study of its kind in the southern United States and the largest population-based health study of African-Americans ever conducted.

The initiative is a collaborative effort of the Vanderbilt Ingram Cancer Center, Meharry Medical College, both located in Nashville, and the International Epidemiology Institute, based in Rockville, Md. The research team will include epidemiologists who are members of the Vanderbilt-Ingram Cancer Center, Vanderbilt's Center for Health Services Research, the Meharry faculty and IEI.

"By determining why African-Americans have higher rates of most forms of cancer, we hope to be able to develop prevention strategies to lower the rates of cancer not only among blacks but among all racial groups," said William Blot, principal investigator. Blot is a member of Vanderbilt-Ingram, a professor of Medicine in Vanderbilt's Division of General Internal Medicine, and a director of IEI.

The Southern Community Cohort Study is being launched to collect information to help prevent cancer and improve its treatment. However, co-principal investigator Margaret Hargreaves noted that its implications are much broader. "This study will allow us to learn more about the association of lifestyle factors to key chronic diseases, such as cancer , cardiovascular disease and diabetes, in residents of the southeastern United States," said Hargreaves, associate professor in Meharry's Department of Internal Medicine.

The study is also expected to yield important health information about low-income and rural populations, regardless of race.

"What excites me about the study is that we will finally get at the 'why' questions implicit in health disparities," said John Maupin Jr., president of Meharry Medical College. "What we haven't known—and what this study will give us—are the reasons why people behave the way they do about their health. Once we have a handle on that, the scientific community will be in a position to develop culturally sensitive interventions to impact health behavior and to have a demonstrable effect on health status and outcomes."

Cohort studies typically enroll large numbers of people and track them over many years for subsequent development of cancer or other diseases. Such studies have yielded much of what is known about the cause and prevention of disease. Some of the better-known cohort studies include the Framingham Heart Study, the Harvard Nurses and Physicians studies, and the American Cancer Society cohort study.

However, these existing cohorts have tended not to include sizeable proportions of African-Americans. Black people comprise only 1-2 percent of the Harvard and ACS studies, for example. In addition, these studies do not include large groups of low-income participants, and except for one study of women in Iowa, have not targeted rural populations.

"Racial, ethnic and socioeconomic disparities in the health of our citizens is a major obstacle in ensuring quality of life for all Americans," said Sen. Bill Frist (R-Tenn.) "These discrepancies will not be solved without the rigorous science to understand each of the variable that contribute to them. I congratulate Meharry Medical College, Vanderbilt-Ingram Cancer Center and the International Epidemiology Insitute for coming together on this pioneering initiative."

As a group, African-Americans face a disproportionate burden from cancer compared to other racial or ethnic groups. According to the American Cancer Society:

—Black women suffer the highest incidence rates of colorectal and lung cancers than other ethnic groups.

—Of any group, black men have the highest incidence rates of prostate, colorectal and lung cancer.

—African-Americans are 33 percent more likely to die of cancer than whites, and twice as likely to die of cancer as Asian/Pacific Islanders, American Indians and Hispanics.

—Black women are more likely to die of breast

cancer and colorectal cancer than any other ethnic group (though white women have the highest incidence of breast cancer).

—Black men are more than twice as likely to die of prostate cancer than men of other ethnic groups.

—Blacks also have higher rates of incidence and mortality from other cancers, including those of the mouth, throat, esophagus, stomach, pancreas and larynx, as well as multiple myeloma.

In addition, the Southeast has some of the highest rates of cancer, among both blacks and whites, in the U.S., for largely unknown reasons, Blot said.

The Southern Community Cohort Study will explore several specific factors that may play a role in the disparities. These variables include the higher-fat "Southern diet" and potential differences in activity levels, body mass index, use of over-the-counter medication use (including aspirin and non-steroidal anti-inflammatory drugs), use of folk and herbal supplements, tobacco use, metabolism of carcinogens and genetic factors.

The study will involve a survey of lifestyle and health history information, follow-up contact every other year, and the optional collection of blood and saliva samples. These samples will be invaluable sources for DNA testing as new genes and proteins are identified and new technologies are developed to identify "markers" of disease risk.

"Laboratory studies using these specimens could make far-reaching contributions to research in cancer, heart disease and other diseases for decades to come," Blot said. "Thanks to what we learn from the life experiences of 40-to-79-year-olds today, the children and grandchildren of this generation may be able to reduce their risks for these diseases in the future."

Information will also be gathered from the federal government's National Death Index and state cancer registries to determine whether individuals in the study have died or been diagnosed with cancer.

The Institutional Review Board at Vanderbilt, which oversees all research at the center involving human subjects, has reviewed and approved the study. The Meharry IRB has also provided initial approval.

Enrollment in the study is expected to begin in early spring at 22 large community health centers in Mississippi, Georgia, Tennessee, South Carolina, Alabama and Florida. In 2004, random telephone sampling will begin in these six states. Hargreaves will be a liaison between the community health centers and the research teams at Meharry and Vanderbilt. Participants must be 40-79 years of age, not currently diagnosed with or under treatment for a terminal illness, and willing to be contacted (and keep in contact with the study coordinators) in the future.

The SCCS collaboration is an outgrowth of the innovative Meharry-Vanderbilt Alliance established in 1999 to promote interaction between the neighboring academic health centers to enhance educational, research and clinical programs at and between both institutions. The multi-year, multi-investigator cohort study will be the largest research endeavor at the Vanderbilt-Ingram Cancer Center.

"This study will provide the in-depth information about causes of cancer that will be critical in the quest to defeat this disease," said Harold Moses, director of the Vanderbilt-Ingram Cancer Center.

For further information about the study, including the list of 22 recruitment sites, visit http://www.southerncommunitystudy.org.

Breast Removal Reduces Risk Of Cancer In BRCA Carriers

A Mayo Clinic study shows that prophylactic removal of both breasts reduces the risk of a subsequent breast cancer by 89.5 percent to 100 percent in women known to be carriers of mutations in the BRCA1 and BRCA2 susceptibility genes.

The study, published in the Nov. 7, 2001, issue of the Journal of the National Cancer Institute followed 26 high-risk women, identified with altered BRCA1 and BRCA2 breast cancer susceptibility genes. All of these women had previously undergone surgery to have their breasts removed. During the period of follow-up thus far, averaging 13.4 years, none of these women have developed breast cancer.

"Calculations predict that six to nine breast cancers should have developed in this group of carriers without prophylactic surgery," said Lynn Hartmann, a Mayo Clinic oncologist and lead researcher on this study. "That translates into a risk reduction of 89.5 percent to 100 percent for bilateral prophylactic mastectomy."

This study is the latest in ongoing research at Mayo Clinic about prophylactic mastectomy and subsequent breast cancer risk. The original research group included 214 women with a strong family history of breast cancer who had previously had prophylactic mastectomy. Women in this surgical group were compared with their sisters who had not had prophylactic mastectomy. That study showed that

prophylactic mastectomy reduced the risk of subsequent breast cancer by approximately 90 percent.

For this most recent study, investigators worked to determine the underlying BRCA1 and BRCA2 status of these high-risk women. Blood samples were obtained from 176 of the 214 women. Twenty-six of these women were identified to have altered BRCA1 and BRCA2 genes and they formed the study group for this JNCI report.

"Our previous study had shown that prophylactic mastectomy reduced subsequent breast cancer risk substantially in women who had the procedure because of a strong family history," Hartmann said. "But a question remained: Would the procedure be able to reduce risk in the highest risk group--namely BRCA1 and BRCA2 carriers? Our current data support that it can, although ours is a relatively small group of carriers. These data complement the Dutch study published this past summer, which showed similar risk reduction in a larger number of carriers who had had prophylactic mastectomy. Their study had a relatively short period of follow-up, however."

Study Underway To Help Childhood Cancer Survivors With Learning Difficulties

A multi-center study based at Oregon Health & Science University's Doernbecher Children's Hospital may help children who survive cancer deal with brain activity deficits resulting from treatment.

The study is funded by a $2.4 million grant from the U.S. National Cancer Institute. Robert Butler, clinical psychologist at Doernbecher and associate professor of pediatrics, OHSU School of Medicine, is leading this research.

The program, known as cognitive remediation, will examine the effectiveness of brain exercises, learning strategies, and cognitive-behavioral therapy.

"Supporting research studies that may lead to the prevention or control of adverse sequela of cancer diagnosis and treatment, and help cancer survivors cope with these possible side effects is one of our key missions," said Noreen Aziz, program director of NCI's Office of Cancer Survivorship.

Learning difficulties often occur in children treated for the most common childhood cancers: leukemia and brain tumors. Patients usually receive radiation treatment, chemotherapy or both to the central nervous system to kill the cancerous cells. Although these treatments save lives, they sometimes impair activities of the brain, such as thinking, attention, memory, speech and flexible thought. Radiation treatment to the brain is more likely to cause the impairment than chemotherapy.

"Now that many children are surviving cancer, pediatric psychologists must take a major role in designing effective rehabilitation programs," Butler said.

In 1990, Butler began working on the problem at Memorial Sloan-Kettering Cancer Center in New York where he received much support for his research. Butler said at that time, "rehabilitation for deficits caused by treatment for childhood cancer was an idea many people at other institutions weren't ready to accept." His early research was funded privately by the Carol Solov Abbani Foundation in New York.

Butler has directed three earlier pilot studies testing the therapy on 33 children. Those studies eventually demonstrated that cognitive remediation may improve attention and concentration skills in most patients. "We don't get rid of all the problems, but we do appear to help," Butler said. "Some kids have been brought pretty close to normal functioning."

As part of the current study, 168 children ages 6 to 17 will be enrolled during the next three years. Participants will undergo 20, two-hour, individualized treatment sessions during a four-to six-month period. The sessions will include exercises and the teaching of new strategies to improve the child's ability to retain information, stay focused and concentrate on problem solving through self-talk. A study therapist monitors the children while they use computer activities, audiotapes and board games. Nationally, 52 children currently are enrolled in the study.

Co-principal investigator on the study is Donna Copeland, Department of Pediatrics, University of Texas, M.D. Anderson Cancer Center, Houston, Texas. Other institutions involved are the Children's Hospital of Philadelphia; University of Rochester; Children's Hospital Los Angeles; St. Jude Children's Research Hospital, Memphis; Children's Hospital Medical Center, Cincinnati; and the AMC Cancer Research Center, Denver.

Protocols Approved During The Month of September 2001

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 below.

Phase I

Phase I Study of Active Immunotherapy with Autologous Dendritic Cells Infected with CEA-6D Expressing Fowlpox-Tricom in Patients with Advanced or Metastatic Malignancies Expressing CEA. Duke University Medical Center, protocol 1864, Lyerly, Herbert, phone 919-681-8350.

Phase I Trial of 2-Methoxyestradiol, an Angiogenesis Inhibitor, in Patients with Solid Tumors. NCI, Medicine Branch, protocol 3371, Dahut, William, phone 301-496-4916.

Phase I Study of ZD1839 (Iressa) in Combination with Irinotecan, Leucovorin, and 5-Fluorouracil in Previously Untreated, Stage IV Colorectal Cancer. Dana-Farber Cancer Center, protocol 3792, Fuchs, Charles, phone 617-632-5840.

Phase I Safety and Pharmacokinetic Study of Squalamine and Carboplatin in Children with Refractory Solid Tumors. Pediatric Oncology Group, protocol ADVL0019, Kieran, Mark, 617-632-4907.

Phase I Study of ZD1839 and Temozolomide for the Treatment of Gliomas. North American Brain Tumor Consortium, protocol NABTC 01-02, Prados, Michael, phone 415-353-2966.

Phase I/II

Phase I/II, Pharmacokinetic, and Biologic Correlative Study of G3139(antisense oligonucletide directed to bcl-2) and Docetaxel in Patients with Hormone-Refractory Prostate Cancer: IND 51,793, Genta-Sponsored IND for Protocol GP202 using G3139. Genta, protocol GP202, Tolcher, Anthony, 210-616-5914.

Pilot and Phase II Trial of Irinotecan and Radiation Followed by Irinotecan and BCNU in Glioblastoma Multiforme Patients. North Central Cancer Treatment Group, protocol N997D, Buckner, Jan, phone 507-284-4320.

Multi-Institutional, Open-Label, Two-Group, Phase II Study of PS-341 in Patients with Advanced or Metastatic Sarcoma. Sloan Kettering Cancer Center, protocol 1757, Maki, Robert, phone 212-639-5720.

Phase II study of Prostatic Acid Phosphatase-Pulsed Dendritic Cells (Provenge) in Combination with Bevacizumab in Patients with Serologic Progression of Prostate Cancer After Definitive Local Therapy. University of California at San Francisco, protocol 2617, Small, Eric, phone 415-353-7095.

Double-Blind, Placebo Controlled Randomized Phase II Trial of Gemcitabine and Cisplatin with or without the VEGF Inhibitor Bevacizumab in Patients with Malignant Mesothelioma. University of Chicago, protocol 2710, Kindler, Hedy, phone 773-702-4400.

Phase II Trial of Gleevec (Imatinib Mesylate, STI-571) in Metastatic Melanoma. M.D. Anderson Cancer, protocol 5345, Eton, Omar, phone 713-794-4633.

Phase II Study of Adoptive Immunotherapy by Allogeneic Stem Cell Transplantation for Metastatic Renal Cell Carcinoma. Cancer and Leukemia Group B, protocol CALGB-90003, Rini, Brian, phone 415-353-7095.

Phase II Study of Gemcitabine, Cisplatin and Radiation Therapy in Patients with Locally Advanced Pancreatic Cancer. North Central Cancer, protocol N9942 Haddock, Michael, phone 507-284-2669.

Phase II Trial Evaluating Multiple Metastasectomy Combined With Hepatic Artery Infusion of Floxuridine and Dexamethasone, Alternating With Systemic Oxaliplatin and Capecitabine for Colorectal Carcinoma Metastatic to the Liver. North Central Cancer Treatment Group, protocol N9945, Bolton, John, phone 504-842-4070.

Phase II Evaluation of Interferon Alpha-2b and Thalidomide in Patients with Disseminated Malignant Melanoma. Southwest Oncology Group, protocol S0026, Hutchins, Laura, phone 501-686-8274.

Phase III/Other

Phase III Randomized Study of Chimeric Anti-GD2 in High Risk Neuroblastoma Following Myeloablative Therapy and Autologous Stem Cell Rescue. Children's Oncology Group, protocol ANBL0032, Yu, Alice, phone 619-543-6844.

Study to Determine the Correlation of Cardiac Function with Patient Characteristics and Blood Markers in Women Enrolled in NSABP-B-31. National Surgical Adjuvant Breast and Bowel Project, protocol NSABP-B-31.1, Romond, Edward, phone 859-323-8043.

MVAC in Organ-Confined Bladder Cancer Based on p53 Status. Southwest Oncology Group, protocol SWOG-4B951, Cote, Richard, phone 323-865-3270.

Validation of a Measurement Method for Intracranial Glial Tumors. North Central Cancer Treatment Group, protocol N007D, Galanis, Evanthia, phone 507-284-3902.