



A PUBLICATION FOR MEMBERS OF THE NORTH CENTRAL CANCER TREATMENT GROUP

Group chair message



Jan C. Buckner, M.D.

At our upcoming fall meeting, we will celebrate the North Central Cancer Treatment Group's (NCCTG) 30th anniversary. In 1977, NCCTG was founded to bring the latest cancer treatments to patients within their own communities. Our success as a cooperative group is largely due to the strong relationship that exists between NCCTG's

research base, Mayo Clinic, and our community members, who participate in all aspects of clinical trial development and provide important feedback as we work to improve our research processes.

We reach the milestone of our 30th anniversary at a challenging time in clinical research. With funding remaining at a constant level and rising costs of clinical research, we are working within NCCTG to improve efficiencies while continuing to develop high-quality clinical trials. We have completed an operations evaluation and have implemented more streamlined processes to reduce the time required for clinical trial development.

Our Imaging Initiative continues to move forward; we have successfully developed and tested software that enables us to transmit images from member sites to the research base. This

program will continue to develop and promises to have a significant impact on the way we incorporate imaging into future clinical research.

This year at the American Society of Clinical Oncology (ASCO) meeting, NCCTG had 37 abstracts accepted, representing all disease areas. (See page 10.) Many of the NCCTG studies presented at the meeting highlight the efforts of our Statistics and Data Center, a group that is responsible for much of the behind-the-scenes work in all aspects of clinical research. In addition to their traditional role of data management and statistical analysis, this group has been at the forefront of improving clinical trial methods and study designs. (See article on page 6.)

We look forward to seeing all members at the fall meeting, where we will come together to learn about new clinical research efforts, discuss future initiatives and celebrate a strong partnership in developing improved cancer therapies.

Jan C. Buckner, M.D.
Group Chair

Fall meeting to celebrate 30th anniversary

Program highlights include:

- Wednesday, Sept. 26, 2007 — NCCTG ASCO Highlights, from 1 to 2:30 p.m., in Presentation Hall, Mayo Civic Center
- Thursday, Sept. 27, 2007
 - Symposium, from 2 to 4:30 p.m., in Presentation Hall, Mayo Civic Center, featuring "A Legacy of Dr. Charles G. Moertel — Progress in the Treatment of Colorectal Cancer," presented by Michael O'Connell, M.D., associate chairman, National Surgical Adjuvant Breast and Bowel Project
 - 30th Anniversary Celebration Reception, from 5:30 to 6:30 p.m., in the Rochester Art Center
 - 30th Anniversary Celebration Dinner and Program, from 7 to 9:30 p.m., in Exhibit Hall A, Mayo Civic Center

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American Society of Clinical Oncology (ASCO) Highlights

The following North Central Cancer Treatment Group (NCCTG) studies were presented at the 2007 American Society of Clinical Oncology (ASCO) meeting.

NCCTG study shows improved progression-free survival for metastatic melanoma patients

New studies being developed to evaluate similar therapies



Svetomir Markovic,
M.D., Ph.D.

At the 2007 American Society of Clinical Oncology annual meeting, NCCTG researchers presented study findings in which two chemotherapy drugs, combined with an agent that prevents the growth of blood vessels, significantly delayed the spread of tumors in patients with metastatic melanoma.



Domingo Perez, M.D.

For 53 patients in this Phase II clinical trial (N047A), tumor growth was delayed by almost six months, whereas typically these cancers demonstrate evidence of significant tumor growth in six to eight weeks after initial diagnosis and with most treatments, researchers say.

“This is the most effective treatment which we have ever tested in NCCTG for this type of cancer, but the results need to be validated,” says Svetomir Markovic, M.D., Ph.D., a Mayo Clinic oncologist and the study’s principal investigator. “It is important for the public to know there is hope for patients with melanoma.”

Melanoma that has metastasized (spread) to other parts of the body is one of the most difficult cancers to treat. Though relatively uncommon, it is also the most deadly form of skin cancer because it does not respond well to chemotherapy. Each year, roughly 8,000 patients die from melanoma and 60,000 new cases are diagnosed.

In this study, researchers combined two chemotherapy drugs — paclitaxel (Taxol) and carboplatin — with bevacizumab, a drug that prevents the formation of new blood vessels and is used to treat cancer in combination with

chemotherapy drugs. The combination of the two chemotherapy drugs has been beneficial in treating other metastatic cancers (e.g., lung cancer and ovarian cancer).

Bevacizumab blocks the vascular endothelial growth factor (VEGF), a substance naturally produced in the body that stimulates the formation of new blood vessels, a process known as angiogenesis. This process is essential for tissue repair, such as wound healing, and for the overall health of the body.

However, VEGF is also important for tumor growth, which depends to a large extent on the formation of new blood vessels to satisfy the increasing oxygen and nutritional needs of the growing tumor. Furthermore, there is evidence that overproduction of VEGF in response to chemotherapy may allow tumors to become more aggressive and resistant to the effects of treatment.

Thus, it was thought that blocking VEGF with a drug like bevacizumab could facilitate the antitumor effects of chemotherapy in patients with metastatic melanoma by disabling the repair mechanism that the tumor would employ in response to the injury from chemotherapy. Bevacizumab is a monoclonal antibody that binds to VEGF and blocks its interaction with cellular receptors. This action prevents new blood vessels from forming and allows the chemotherapy to work.

Researchers stress the need for continued research to further examine the effectiveness of these and other therapies. “The clinical benefit may seem small, but in the world of melanoma where there is very little progress, this is certainly a strong indication that the combination of chemotherapy with an antiangiogenic agent may be a valid treatment strategy for these patients,” says Domingo Perez, M.D., lead author of the study who is a former oncology fellow at Mayo Clinic and is now in private practice in Minneapolis. “But the only way to know this for certain is a head-to-head comparison with the standard course of treatment.”

Several studies are under way to further explore the process observed in N047A. “In upcoming studies, we are going to examine both the toxic injury to cancer and the angiogenesis repair



mechanism in different ways," says Dr. Markovic. "We will evaluate different agents and test therapies that had not worked in the past because of the angiogenesis repair of the tumor."

A new NCCTG trial, N0675, is a Phase II trial to test the combination of temozolomide, a chemotherapy drug, and RAD001, a different angiogenesis inhibitor drug for the treatment of metastatic melanoma.

Clinical trial VF4096G is a new study based on the initial results of N047A and originated by Genentech Corporation (manufacturer of bevacizumab). In this trial, Mayo Clinic is partnering with Genentech to evaluate the effectiveness of paclitaxel and carboplatin versus paclitaxel and carboplatin and bevacizumab. This trial directly evaluates the benefit of adding bevacizumab to the two chemotherapeutic agents by comparing the ability of the two- and three-drug combinations to prolong progression-free survival in patients with metastatic melanoma.

Both N0675 and VF4096G will open for enrollment during the third quarter of 2007. Several other Phase I and Phase II trials are also under development and will be available for enrollment by the spring semiannual NCCTG meeting in 2008.

For more information on the above clinical trials, visit the NCCTG Web site at <http://ncctg.mayo.edu>.

Vorinostat shows anticancer activity in recurrent gliomas

Researchers to continue testing targeted therapies to treat gliomas

A NCCTG study finds that a novel application of the drug vorinostat shows activity in patients with recurrent glioblastoma multiforme. Vorinostat is the first U.S. Food and Drug Administration-approved oral anticancer drug that inhibits an enzyme, histone deacetylase, which is closely associated with DNA in cells. By inhibiting the deacetylation of histones — proteins that help organize the structure of DNA — vorinostat stops tumor growth. Study results were presented at the American Society of Clinical Oncology annual meeting in June 2007 by Evanthia Galanis, M.D., a Mayo Clinic oncologist and lead investigator of the study.



Evanthia Galanis, M.D.

Glioblastoma multiforme is a lethal primary brain tumor. The average survival of glioblastoma patients is 12 to 16 months. These tumors recur quickly, despite multimodality treatment. Treatment options are limited at recurrence, and patients survive for an average of three to four months.

"Existing treatment interventions have minimal impact on the outcome for patients with recurrent glioblastoma multiforme," says Dr. Galanis. "Using vorinostat to treat glioblastoma multiforme patients who have relapsed following surgery, radiation and chemotherapy, we found that 15 percent of the patients had no tumor recurrence for six months or longer following treatment initiation. The median overall survival of the patients enrolled on the trial was 5.7 months — similar patient populations enrolled in prior NCCTG trials had a median overall survival of between 4 and 4.4 months."

An additional group of patients in this study was treated with vorinostat prior to surgery, and a gene and protein analysis of their resected tumors was performed. This analysis confirmed that vorinostat alters the expression of several important genes and proteins, indicating that the drug effectively reaches its target in the central nervous system tumor.

Dr. Galanis says the researchers plan to expand this genetic analysis to all study patients. This will help define a patient population that has a higher likelihood of benefiting from treatment — allowing treatment individualization in the future.

NCCTG members have played an important role in making this genetic analysis possible, says Dr. Galanis. Member sites were asked to submit several blood and tissue samples for each participant. These samples will be used to continue the correlative laboratory analysis phase of the study.

Future NCCTG clinical trials will build on this initial promising data. Studies in development will investigate the effectiveness of vorinostat in combination with other therapies such as radiation therapy, temozolomide, and other small-molecule cell cycle inhibitors in treating patients with newly-diagnosed or recurrent glioblastoma multiforme.



Ginseng shows potential to reduce cancer-related fatigue

Positive pilot study results will lead to further research



Debra Barton, Ph.D.

Extreme fatigue is a problem many cancer patients face after diagnosis and during treatment. Getting more sleep or rest often does not relieve the fatigue, nor is it related to activity levels. Besides exercise, there isn't a good solution available for these patients.

However, a pilot study conducted by North Central Cancer Treatment Group (NCCTG) researchers shows that a form of American ginseng provides greater improvements in fatigue and vitality in patients who receive the highest doses tested, compared to a lower dose or placebo.

Study results were presented at the 2007 American Society of Clinical Oncology annual meeting in June. The study was the first to test the Wisconsin species of American ginseng as a possible therapy for cancer-related fatigue.

"We hope that Wisconsin ginseng may offer us a much-needed treatment to improve cancer patients' quality of life and we look forward to further evaluation of this therapy," says Debra Barton, Ph.D., a registered nurse, Mayo Clinic cancer researcher and the study's primary investigator.

Study background

"Cancer-related fatigue is one of the most profound and distressing issues patients face," says Dr. Barton. This unique type of fatigue can have dozens of reasons for occurrence. According to Dr. Barton, another study showed that patients who were diagnosed a year prior and completed cancer therapy, still reported fatigue as one of their foremost concerns, second only to fear of disease recurrence.

Traditional Chinese medicine and current understanding of ginseng's function both point to its characteristics as an adaptogen — a substance that helps the body overcome the effects of environmental stress. Since cancer patients have stressors ranging from the psychological stress of diagnosis to the physiological stresses of chemotherapy and radiation, if ginseng helps, the

researchers believe it would be a valuable addition to currently available therapies.

"With animal studies indicating that ginseng could help to increase endurance, and the availability and verified product quality of Wisconsin ginseng, we decided to move forward with a pilot study," says Dr. Barton.

Study methodology and results

The purpose of the pilot study was to pinpoint which aspects of fatigue ginseng might help alleviate, determine likely dosage options and identify possible side effects. Investigators enrolled 282 patients in the randomized, placebo-controlled trial. An average of 71 patients were assigned to each arm, with between 39 and 48 patients in each arm completing the eight weeks of treatment. Treatment arms consisted of placebo, and three different daily doses of Wisconsin ginseng — 750, 1,000 and 2,000 milligrams.

Study results indicated that patients receiving the placebo and the lowest dose of ginseng reported very little improvement in fatigue, vitality or other areas of physical or psychological well-being. The patients receiving the larger doses, 1,000 milligrams per day and 2,000 milligrams per day, showed improvements in overall energy levels, reporting higher vitality levels and less interference with activity from fatigue. These patients also reported an improvement in overall mental, physical, spiritual and emotional well-being.

Because this was a pilot study, Dr. Barton cautions against immediate addition of ginseng supplements to any patient's therapeutic regimen. "While results were promising, we have more research to conduct," she says.

Dr. Barton's research team plans to open a new clinical trial in 2008 to evaluate 1,500 milligrams per day of Wisconsin ginseng versus placebo in hopes of confirming a new treatment option for cancer-related fatigue.

Researchers test interventions to eliminate epidermal growth factor receptor (EGFR) inhibitor-induced skin rash

In cancer therapy, epidermal growth factor receptor (EGFR) inhibitors are increasingly being used to treat a broad range of malignancies including head and neck cancer, lung cancer and



gastrointestinal cancer. Up to 70 percent of patients treated with EGFR inhibitors experience a skin rash that spreads over the body and on the face.



Aminah Jatoi, M.D.

“As clinicians, we see that patients are bothered by the appearance and discomfort of the rash,” says Aminah Jatoi, M.D., an oncologist at Mayo Clinic in Rochester, Minn. and lead investigator for several NCCTG studies in symptom management. “As drugs like EGFR inhibitors are being used increasingly more often in the clinic, NCCTG is committed to finding ways to manage side effects and to improve the quality of life of cancer patients.”

Clinical trial N03CB was the first NCCTG trial to test therapy for the EGFR inhibitor-induced skin rash. In the Phase III, double-blind study, 61 patients were randomly assigned to tetracycline twice daily for four weeks or a similarly designed placebo for the same time period. Researchers selected to test

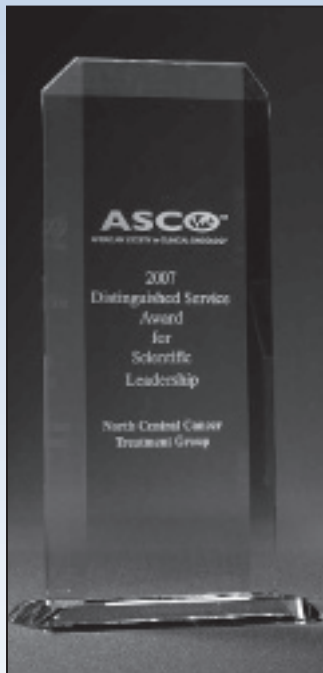
tetracycline because of anecdotal reports that it could be used to treat this acne like rash.

Researchers found that tetracycline did not reduce rash incidence but may impact rash severity. To confirm these findings, a follow-up study is under way using the same methods.

In addition, NCCTG researchers have developed another study, clinical trial N05C4, to test the effectiveness of sunscreen in reducing the EGFR inhibitor-induced rash. Previous research shows that light may play a role in increasing the severity of the skin rash. Therefore, this trial is designed to test the effectiveness of sunscreen in reducing light exposure that may make the rash worse. This Phase III, randomized, double-blind, placebo-controlled trial has almost reached its accrual goal of 110 patients.

“This next-generation sunscreen study is moving forward at a brisk pace with results promising to be available in 2007,” says Dr. Jatoi. “Our goal is to understand the underlying biological causes of this rash so that we can develop better therapies for patients who must confront this upsetting side effect.”

American Society of Clinical Oncology (ASCO) Awards



North Central Cancer Treatment Group (NCCTG) among Cancer Cooperative Groups honored

The North Central Cancer Treatment Group (NCCTG) was one of 12 National Cancer Institute Cancer Cooperative Groups to receive the 2007 Distinguished Service Award for Scientific Leadership from the American Society of Clinical Oncology (ASCO) at the group’s June meeting. Jan C. Buckner, M.D., group chair for NCCTG, along with representatives from the other Cancer Cooperative Groups, accepted the award, which recognizes each group’s efforts to design and conduct clinical trials, many of which have led to the development of new cancer treatments.

Two NCCTG member sites recognized for clinical trials participation

At the June 2007 ASCO meeting, two NCCTG members — Duluth Clinic Cancer Center in Duluth, Minn. and Oncology Hematology Associates of Central Illinois in Peoria — were among the recipients of the 2007 Clinical Participation Awards. Daniel Nikcevich, M.D., from the Duluth membership and John Kugler, M.D., from the Peoria membership accepted the awards. ASCO created the award in 2003 as a mechanism to publicly honor community-based oncology practices that actively participate in clinical trials research.



North Central Cancer Treatment Group (NCCTG) Statistics and Data Center

Playing a critical role in clinical trials, helping to shape future research efforts



Daniel Sargent, Ph.D.

The North Central Cancer Treatment Group (NCCTG) Statistics and Data Center (SDC) plays a critical role in the development, activation and analysis phases of NCCTG clinical trials. Since NCCTG's inception in 1977, the Statistics and Data Center has provided statistical data management and information technology development and

implementation for clinical research.

"Our goal is to collaborate with investigators, physicians and nurses within NCCTG to provide efficient and effective methods for conducting clinical research," says Daniel Sargent, Ph.D., a statistician at Mayo Clinic and group statistician for NCCTG. "We want to collect the right data to answer the important research questions so that we can make new medical treatments available to patients as quickly as possible."

The SDC is comprised of 25 statisticians from Mayo Clinic, NCCTG's research base. These statisticians are part of the 45 statisticians in the Mayo Clinic Cancer Center and a subset of the more than 200 biostatisticians at Mayo Clinic. This larger network enables the SDC team to share resources and knowledge in designing and implementing clinical research.

Statisticians within the SDC work with specific investigators, specializing in a particular disease area. NCCTG statisticians become part of the research team and learn about the particular disease being treated as well as the different therapies being tested in clinical trials. Because of this involvement, they can better assist investigators in developing the best clinical trial design to evaluate new treatments.

"Our Statistics and Data Center is recognized within the research community as an outstanding component of NCCTG, staying at the forefront of clinical research design and methodology," says Jan C. Buckner, M.D., an oncologist at Mayo Clinic and the NCCTG group chair. "Our statisticians collaborate with NCCTG investigators and our community physicians and nurses to develop efficient, high-quality research tools."

Quality Assurance

The SDC plays an important role in assuring the quality of clinical trial data collection and providing efficient methods for data submission. An important tool in this effort has been the development and implementation of a Remote Data Capture System for clinical trials patient registration and patient data submission. This Web-based system enables staff at NCCTG member sites to register patients online as well as submit required information during the clinical trial.

"The Remote Data Capture System also includes an electronic editing function that prompts members if incorrect data is entered," says Dr. Sargent. "The NCCTG membership has embraced the remote data system because it provides real-time feedback on data entry errors and also provides a convenient tool for submitting patient information. In addition, member sites can monitor their data submission requirements by looking online for a list of upcoming data report deadlines. They can search for data requirements for their site, for a particular clinical trial or for a specific clinical trial participant."

Prior to the development of the Remote Data Capture System, member site staff submitted patient registration and clinical trial data via paper forms that were mailed to the research base. Once the NCCTG staff processed the forms, they contacted sites to correct any data entry errors. This process was time-consuming and cumbersome. The Remote Data Capture System provides higher-quality data submitted in a timely manner, explains Dr. Sargent.

Piloted for several studies beginning in 2003, the Remote Data Capture System has been implemented for all NCCTG clinical trials during the past year. Statisticians worked with the NCCTG clinical research associates and nurses to develop and test the system. This collaboration helped to create a user-friendly data collection and management system to fit the needs of member sites.

Clinical Trials Methodology

Just as NCCTG investigators test cancer treatments before they become standard therapy, NCCTG statisticians evaluate new statistical and



analytical methods that, if proven effective, can improve the clinical research process.

“In addition to the traditional roles of a cooperative group statistics center, the SDC, working in collaboration with the NCCTG scientific committees, has contributed substantially to the understanding of clinical trials processes and study endpoints,” says Dr. Sargent. “The SDC has conducted research into clinical trials methodology, making use of NCCTG data and expertise to explore real-world issues in clinical trials. The purpose of this methodology research is to improve efficiency, reduce the amount of data collected, improve patient safety and define novel endpoints for the conduct of NCCTG and other clinical trials.”

The following sections highlight the SDC research activities in adverse event reporting, tumor response assessment and endpoint analysis.

Adverse event reporting

The reporting of an adverse event for a clinical trial participant — any side effect which a patient experiences during treatment — is a critical and time-consuming aspect of clinical research. Adverse events are graded on a scale of 1 (mild side effects) to 5 (an adverse event that results in patient death). The SDC has completed several research projects to assure that the data essential to protect patient safety is collected, while minimizing the burden on local NCCTG sites. To address this issue, the SDC examined the methods used to report adverse events, the types of adverse events being reported and the reported cause of adverse events.

NCCTG statisticians recognized a need to communicate quickly with investigators and clinical study staff when serious adverse events occurred for clinical trial participants. Therefore, the group developed the NCCTG Real Time Adverse Event Monitoring System. The system allows member site staff to complete a one-page form online to report any adverse events experienced by a participant in a NCCTG clinical trial. Each day, these reports are compiled and forwarded to the clinical trial investigator and statistician working on the trial. This allows investigators to closely monitor adverse events and make any necessary modifications in treatment.

Statisticians also conducted a detailed analysis of adverse event data submitted on NCCTG clinical trials from 1999 to 2001, and determined that a great deal of time and expense were being used to collect information that was of limited value, as this data

did not result in any change to a treatment regimen and was typically not reported in a manuscript. As a result of this analysis led by Michelle Mahoney, SDC proposed and NCCTG adopted a new policy for adverse event reporting which states that all grade 1 adverse events and grade 2 events that are not related or unlikely related to treatment need not be reported to the SDC.



Michelle Mahoney

In addition, NCCTG statisticians have examined the value of reporting attribution — the suspected cause of the adverse event — in conducting the final analysis on clinical trial data. To examine this question, Shauna Hillman, an NCCTG statistician, reviewed results from the placebo arm of completed clinical trials.



Shauna Hillman

Hillman discovered that more than 50 percent of adverse events reported were attributed to the therapy, in these cases a placebo, which clearly was an error, as the placebo pill should have no physiological effect on the patient. In these trials, physicians had incorrectly attributed a side effect to a placebo pill, pointing to the difficulty of assigning attribution of adverse events to any treatment.

Based on this study, NCCTG has recommended to the National Cancer Institute (NCI) that adverse event attribution data not be collected for randomized trials.

Hillman reported these results at the American Society of Clinical Oncology (ASCO) meeting in June and received favorable feedback from investigators and clinical research associates who are responsible for collecting adverse event data.

Tumor response assessment

In 2000, NCI initiated the Response Evaluation Criteria in Solid Tumors (RECIST) guidelines for assessing tumor response that required all lesions, up to 10 lesions, be measured and recorded for each clinical trial participant at every evaluation. NCCTG statisticians undertook a detailed analysis of tumor measurement data from completed clinical trials.



Based on a variety of analyses, the research team concluded that measuring two lesions as opposed to 10 would not substantially impact trial results. NCCTG statisticians have communicated these results to the international RECIST committee for consideration in the revised RECIST guidelines which are under development.

Endpoint analysis

The SDC has also led several large pooled analyses exploring endpoints in cancer clinical trials. In this type of evaluation, statisticians examine whether current time frames for measuring treatment success can be reduced so that tested therapies can be available to all patients sooner. NCCTG investigators have conducted endpoint analysis in the areas of colon cancer, neuro-oncology and melanoma.

To further research in colon cancer, Dr. Sargent founded the Adjuvant Colon Cancer Endpoints Group (ACCENT) in 2003, bringing together members from all cooperative groups in the United States as well as investigators from around the world. Through this collaboration, researchers have been able to combine data from national and international colon cancer trials and create a database of almost 21,000 patients.

In study N0441, NCCTG statisticians and members of the ACCENT group used this database and examined the endpoint for evaluating adjuvant colon cancer treatments. "We wanted to address the hypothesis that disease-free survival, assessed after a median of three years of follow-up, could replace overall survival after five years of follow-up, the standard time frame for evaluation," says Dr. Sargent. "Based on multiple analysis techniques, ranging from simple to very complex, every analysis was consistent in supporting three-year disease-free survival as a valid endpoint."

Dr. Sargent and his team presented this data to the Oncologic Drugs Advisory Committee of the Food and Drug Administration. The committee voted unanimously to accept three-year disease-free survival as an endpoint to permit full regulatory approval in adjuvant colon cancer.

"These findings are very important," says Dr. Buckner. "They significantly reduce the amount of time required to evaluate a drug, and therefore, allow clinical researchers to test therapies in a shorter time period and make them available to all patients sooner."

Dr. Sargent's research team continues to examine the colon cancer endpoints and recently completed an analysis to be published in the *Journal of Clinical Oncology* that suggests two years is also an acceptable evaluation time frame.

Future colon cancer research objectives using the pooled data from N0441 include:

- Evaluate patients who have a late recurrence of their colon cancer and identify if there are any characteristics that predict this condition
- Examine the effectiveness of chemotherapy for colon cancer in elderly patients
- Develop a tool to aid researchers in designing colon cancer clinical trials with the appropriate endpoint evaluation

In addition, the ACCENT team has received a commitment from investigators of five large colon cancer trials completed in the last five years to contribute their data to the ACCENT database.

Similar research has been conducted by SDC in neuro-oncology. For example, commonly used endpoints for Phase II glioblastoma multiforme (GBM) trials are the percentage of patients who are progression-free at six months and the percentage of patients who are alive at 12 months. In an effort to identify the best endpoints for these trials, Karla Ballman, Ph.D., analyzed the relationship in past NCCTG trials between these endpoints separately for newly diagnosed GBM trials and recurrent GBM trials. Results indicated that for recurrent GBM, six-month progression-free survival was a valid endpoint for evaluation, and in newly diagnosed GBM, 12 months was still the best evaluation time frame.



Karla Ballman, Ph.D.

Study Design

As with clinical trial methodology, NCCTG statisticians have also had a strong interest in developing optimal study designs to evaluate new treatments efficiently in the shortest time.

NCCTG statisticians have developed study design models for many research scenarios including:

- Models for Phase I studies that determine the maximum tolerated dose for therapies in less time than standard trial designs



- Study designs that allow Phase II clinical trials to be conducted using 20 percent fewer patients
- Methods for designing a Phase III trial where the objective is to identify which patients will benefit from a given therapy based on their genetic characteristics

Focusing on better techniques for future research

NCCTG statisticians continue to be leaders in quality assurance, clinical trial methodology and study design within the cancer research community. Through efforts like the ACCENT group, NCCTG

collaborates with other researchers to identify the best methods to answer important therapeutic questions efficiently and effectively.

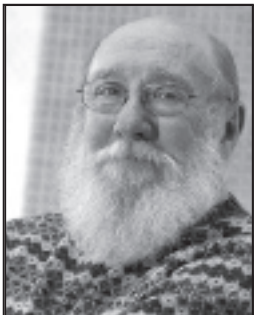
“A consistent theme of all SDC research is to make clinical trials more efficient, less burdensome, and whenever possible, able to accomplish the scientific goals with a smaller number of patients,” says Dr. Sargent. “The NCCTG SDC is committed to continuing our strong tradition of collaboration, clinical trials research, and statistical methodologic research to meet the challenges of the ongoing rapid evolution of cancer research.”

NCCTG 5th Annual Patient Advocate Symposium held in June
An update from Cynthia Chauhan



Cynthia Chauhan

The NCCTG Patient Advocacy Committee hosted its 5th annual Patient Advocate Symposium, June 11 to 13. The symposium was conceived and developed as a way to offer education and support to community advocates and enable advocates from the NCCTG community sites to come together and learn from each other in a congenial environment. Cynthia Chauhan and Wayland Eppard, co-chairs of NCCTG’s Patient Advocacy Committee, organized the symposium.



Wayland Eppard

NCCTG patient advocates in the community setting have a unique and especially important role. They are survivors and caregivers who support the community cancer centers in reaching out to new patients and offering support through the diagnosis and treatment phases of the cancer journey.

Thirty people from 10 states attended the symposium to learn about NCCTG and the role of clinical trials in advancing cancer treatment, to meet

cancer researchers, to sharpen their skills and to network with each other. Learning about NCCTG and clinical trials helps community advocates to answer general questions other patients might have. Learning directly from researchers about their work gives community advocates firsthand knowledge of the commitment and dedication of these professionals. At the same time, the research professionals have the opportunity to talk with patients who benefit from their work and to share their concerns about the future of research with a group of dedicated, active volunteers.

Advocates attending this symposium had an opportunity to work on their public speaking skills, their writing skills, and to brainstorm new avenues for reaching and supporting patients. Networking is an important part of the symposium as advocates share their volunteer experiences and ideas with each other, offering support and stimulation.

The Patient Advocate Symposium is an opportunity for advocates to step back from their community work and survey the incredible impact they have on the lives of others as they give from their hearts to the well-being of fellow patients. At the same time, they stimulate each other to expand their activities in new directions to help support fellow patients and educate the communities in which they live to the importance of cancer clinical trials in the continuum of cancer care.



North Central Cancer Treatment Group (NCCTG) Abstracts for ASCO 2007

Neuro-oncology

N047B — North Central Cancer Treatment Group (NCCTG) Phase II trial of vorinostat (suberoylanilide hydroxamic acid, SAHA) in recurrent glioblastoma multiforme — *Presenter: Evanthia Galanis, M.D., oral presentation*

N0678 — Joint North American Brain Tumor Consortium and NCCTG prognostic factors analysis for high-grade recurrent glioma — *Presenter: Wenting Wu, Ph.D., poster*

Breast

E1199 — Phase III study of doxorubicin-cyclophosphamide followed by paclitaxel or docetaxel given every 3 weeks or weekly in patients with axillary node-positive or high-risk node-negative breast cancer —

Presenter: Joseph Sparano, M.D., oral presentation

N9831 — Updated results of the combined analysis of NCCTG N9831 and National Surgical Adjuvant Breast and Bowel Project B-31 adjuvant chemotherapy with/without trastuzumab in patients with HER2-positive breast cancer — *Presenter: Edith Perez, M.D., oral presentation*

MA.17 — Competing causes of death in National Cancer Institute of Canada Clinical Trials Group MA.17, a placebo-controlled trial of letrozole as extended adjuvant therapy for breast cancer patients —

Presenter: Judy-Anne Chapman, Ph.D., poster

N0234 — Translational correlates, including outcome for patients with ER-/PR-/HER2-(triple negative) disease from N0234, a Phase II trial of gemcitabine and erlotinib for patients with previously-treated breast cancer —

Presenter: Timothy Hobday, M.D., poster

N0531 — NCCTG Phase II trial of weekly nab-paclitaxel in combination with gemcitabine in patients with metastatic breast cancer — *Presenter: Vivek Roy, M.D., poster*

MA.21 — A sequential Phase III adjuvant trial of sequenced EC plus filgrastim plus epoetin alfa followed by paclitaxel versus sequenced AC followed by paclitaxel versus CEF in women with node-positive or high-risk, node-negative breast cancer. — *Presenter: Margot Burnell, M.D., poster*

N9831 — A correlative study of cardiac biomarkers and left ventricular ejection fraction from N9831, a Phase III randomized trial of chemotherapy and trastuzumab as adjuvant therapy for HER2-positive breast cancer —

Presenter: Leila Kutteh, M.D., poster

N9831 — Impact of poor prognostic features on the surgical treatment of breast cancer in a large cooperative group trial — *Presenter: Barbara Pockaj, M.D., poster*

S0012 — Screening for clonal hematopoiesis as a predictive marker for development of t-AML following adjuvant therapy for breast cancer — *Author: Marilyn Slovak, Ph.D., publication*

Cancer Control

N00CB — Gabapentin for hot flashes in men — *Presenter: Charles Loprinzi, M.D., oral presentation*

N03CA — A pilot, placebo-controlled evaluation of American Ginseng (*panax quinquefolius*) to improve cancer-related fatigue — *Presenter: Debra Barton, Ph.D., oral presentation*

N03CB — Does tetracycline prevent or palliate epidermal growth factor receptor (EGFR) inhibitor-skin rash? — *Presenter: Aminah Jatoi, M.D., oral presentation*

Gastrointestinal Malignancies

90-47-51 (Intergroup 0114) — Ratio of metastatic to examined lymph nodes a powerful predictor of overall survival in rectal cancer: an analysis of Intergroup 0114 — *Presenter: Michael Meyers, M.D., oral presentation*

N0441 — Survival following recurrence in patients with adjuvant colon cancer: findings from the 20,800 patient ACCENT dataset — *Presenter: Michael O'Connell, M.D., oral presentation*

N0441 — Time dependent patterns of failure and treatment benefit from adjuvant therapy for resectable colon cancer: Lessons from the 20,800 patient ACCENT dataset — *Presenter: Daniel Sargent, Ph.D., oral presentation*

N0545 — A pooled safety and efficacy analysis examining the effect of performance status on outcomes in nine first-line treatment trials of 6,286 patients with metastatic colorectal cancer — *Presenter: Richard Goldberg, M.D., oral presentation*

N0442 — Mutations in the proapoptotic VAX gene are associated with defective DNA mismatch repair and altered tumor growth rates in human colon cancers — *Presenter: Frank Sinicrope, M.D., poster discussion.*

N0441 — Outcomes in patients of African descent and white patients receiving adjuvant therapy for colon cancer — *Presenter: Greg Yothers, Ph.D., poster discussion*

N9741 — Waterfall plots provide detailed information on magnitude of response to conventional chemotherapy in advanced colorectal cancer — lessons learned from N9741 — *Presenter: Megan Campbell, poster discussion*

N0341 — Phase II trial of oxaliplatin, irinotecan, 5-fluorouracil, and leucovorin for metastatic colorectal cancer — *Presenter: Robert McWilliams, M.D., poster (GI ASCO)*

N0349 — Phase II study of oxaliplatin, 5-FU and RT followed by gemcitabine in patients with unresectable pancreatic cancer — *Presenter: Michael Haddock, M.D., poster (GI ASCO)*

N044J — NCCTG Phase II trial of AZD2171 for patients with hepatocellular carcinoma — interim review of toxicity — *Presenter: Steven Alberts, M.D., poster (GI ASCO)*

N034A — Phase II trial of bevacizumab, gemcitabine, oxaliplatin in patients with metastatic pancreatic adenocarcinoma — *Presenter: George Kim, M.D., poster (GI ASCO)*

N9741 — Survival update and prognostic factor analysis of oxaliplatin and irinotecan combinations for metastatic colorectal cancer — *Presenter: Hanna Sanoff, M.D., poster.*

N9943 — NCCTG Phase I/II trial of gemcitabine and pemetrexed in patients with biliary tract or gallbladder carcinoma — Phase II results — *Presenter: Robert McWilliams, M.D., poster (GI ASCO and ASCO)*

N9945 — Systemic capecitabine and oxaliplatin administered with hepatic arterial infusion of floxuridine following complete resection of colorectal metastases confined to the liver: final results of a NCCTG Phase II inter-group trial — *Presenter: Steven Alberts, M.D., poster*

N0442 — EGFR expression is associated with increased cell turnover and poor histologic grade in human colon carcinomas — *Author: Rafaela Rego, M.D., publication (GI ASCO and ASCO)*

Lung Cancer

N0326 — A front-line “Window of Opportunity” Phase II study of sorafenib in patients with advanced non-small cell lung cancer — *Presenter: Alex Adjei, M.D., Ph.D., poster discussion*

N0424 — Age, gender, performance status and stage outperformed stage alone in predicting overall survival (OS) in patients with small cell lung cancer: a pooled analysis of 1,623 patients from the North Central Cancer Treatment Group — *Presenter: Nathan Foster, poster*

90-24-51 and 94-24-51 — The value of combined modality therapy in elderly patients with stage III non-small cell lung cancer — *Author: Steven Schild, M.D., publication*

Novel Therapeutics

N0377 — Results of NCCTG Phase II trial of the mTOR inhibitor iverolimus in metastatic melanoma — *Presenter: Ravi Rao, M.B.B.S., poster discussion*

N0071 — Aerosolized sargramostim for the treatment of metastatic melanoma to the lungs — *Presenter: Svetomir Markovic, M.D., Ph.D., poster*

N047A — Phase II trial of carboplatin, weekly paclitaxel, and biweekly bevacizumab in patients with unresectable stage IV melanoma — *Presenter: Domingo Perez, M.D., poster*

Statistics

97-24-51 — Questionable value of attribution when interpreting adverse event data: A joint evaluation by North Central Cancer Treatment Group (NCCTG) and American College of Surgeons Oncology Group (ACOSOG) — *Presenter: Shauna Hillman, oral presentation*

Prognostic significance of patient-physician disagreement about performance status in patients with advanced cancer — *Presenter: Ian Schnadig, M.D., poster discussion*



Spring 2007 North Central Cancer Treatment Group Meeting Highlights

Symposium



Bradley Erickson, M.D., Ph.D., presents "The Role of Imaging in the Age of Genomics" at the spring symposium.

Clinical Research Associate (CRA)/Nurse Workshop



Lynn Flickinger, a protocol development coordinator for the NCCTG Breast Program (at left) and Jeannine Hadley, supervisor of the NCCTG Protocol Development Unit, present upcoming breast cancer studies to clinical research associates and nurses from the NCCTG member sites.



Marie Christine Aubry, M.D., a Mayo Clinic pathologist and director of the NCCTG Biospecimen Resource, presents the translational research components of upcoming breast cancer trials to NCCTG members.



Fran Palmieri, a clinical nurse specialist at Mayo Clinic, discusses patient education material for upcoming breast cancer trials.

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Future Meeting Dates

April 7–10, 2008 • Oct. 20–23, 2008