



# THE CAL·GAB

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## IN THIS ISSUE:

### ■ Message from the Chair ..... p. 2

The future of a national clinical trials program in cancer research is secure. Dramatic changes will be seen, however, in the way cooperative groups conduct clinical trials. *Richard L. Schilsky, M.D.*

### ■ CALGB Group News

#### Cooperative Group Clinical Trials Program Changes ..... p. 1

Pilot projects by the NCI, NCI Cooperative Groups, CALGB and SWOG come on-line in 1999 to evaluate changes in how clinical trials are developed and conducted.

- Clinical Trials Implementation Committee Roll-out ..... p. 5
- CALGB/SWOG CCOP Pilot Project ..... p. 4
- CALGB Centralized IRB Pilot ..... p. 4

#### Group News Highlights ..... p. 3

- Leadership changes in Transplant and Lymphoma Committees
- GI study goes multinational
- New PIs named at Wake Forest and Walter Reed
- Two CCOPs choose CALGB as second major CCOP research base
- Group Meeting news and announcements

### ■ Fall Group Meeting Report

#### Presentations on Cancer in the Elderly ..... p. 6

#### Oncology Nursing Presentation on Melanoma ..... p. 8

### ■ Operations, Data Management, and Information Systems

An expanded section on important changes and developments affecting data reporting and information access.

- Government Initiatives—New Data Update System ..... p. 10
- Data Reduction ..... p. 10
- Physician Group Membership Category Created ..... p. 11
- Client Rollout and On-Line Patient Registration ..... p. 12
- Quality Assurance—Administrative Database ..... p. 12
- QA—Scientific: Barcode System for Forms Tracking ..... p. 13
- Automate Administrative Tasks—Web Site Enhancements ..... p. 13

### ■ Protocol News ..... p. 14

- Protocol updates
- New and closed studies
- Current funding available

## Changes to Cooperative Group Clinical Trials Impact CALGB

**Several new pilot programs and initiatives to streamline and improve the clinical trials process nationwide will have significant impact on how protocols are initiated and conducted by CALGB institutions and researchers.**

**If successful, these programs will blur the boundaries between existing cooperative groups, and increase accrual by making it easier to enroll patients on protocols.**

### Clinical Trials Implementation Committee Recommendations

A comprehensive program to improve the national clinical trials program will be tested first in new lung and GU cancer studies beginning this year.

Researchers from NCI cooperative groups and other research organizations nationwide will develop concepts for Phase III studies. The best protocol concepts will be selected by peer review committees and opened to accrual by all cooperative groups. Changes will be tested in many of the processes of developing and implementing multi-center phase III trials, from initial strategies to final implementation. Beginning later this year, researchers in **lung** and **GU cancers** will participate in the trial program. *(Details, page 5)*

### Cooperative Groups to collaborate on open protocols in GI cancer and Leukemia

Similar to the innovations to the national clinical trials program being tested in lung and GU cancer, the NCI cooperative groups will convene strategy meetings to collaborate on the development of new studies in GI cancer and Leukemia. Protocol concepts will be reviewed by the NCI Cancer Therapy Evaluation Program. Once approved, they will be opened for accrual to all cooperative groups.

*Overview continued on page 4*

### Cancer and Leukemia Group B

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## MESSAGE FROM THE CHAIR

# The future of clinical cancer research

As we enter the final year of the 20th century, the cooperative group program, and CALGB in particular, are poised to initiate dramatic changes in the way we conduct clinical

cancer research. This issue of the *CAL•GAB* summarizes many of the changes in the organization and procedures of the cooperative groups that have been devised to enhance the productivity, efficiency, flexibility and quality of this highly successful enterprise. The overall goals are to develop the best possible research studies, complete accrual and analysis as quickly as possible and disseminate research results as broadly

as possible so that our patients have the most information and greatest array of options available to assist them in making informed choices.



*Richard L. Schilsky, M.D.*

### Identifying and supporting the best science

Beginning later this year, NCI will convene concept evaluation panels (CEPs) to provide peer review of all concepts for phase III trials in the areas of GU and lung cancer. The multi-disciplinary CEPs will review proposals from cooperative groups, cancer centers, SPOREs and other sources. The most meritorious concepts will be selected for protocol development and the final protocol will be available to all cooperative groups and qualified investigators. The sponsoring group or organization will retain final responsibility for protocol analysis and publication of results.

Supplemental "leadership funds" will be provided by NCI to support the conduct of these studies. If successful, this review process will be extended to other disease areas.

### Broadening the menu of protocol options

As described above, phase III trials in GU and lung cancer that are approved by the CEP will be conducted as intergroup protocols. To further expand the menu of studies available to community physicians, the Division of Cancer Prevention at NCI has initiated a pilot program to permit CCOPs to participate in more than one multi-disciplinary cooperative group. As a result, two new CCOPs will join CALGB and will have available the full range of CALGB protocols. CALGB and SWOG have also initiated a pilot program to make selected SWOG protocols available to all CALGB CCOPs. This program will provide CALGB CCOPs with protocols in disease areas not studied by CALGB, such as brain tumors and sarcomas.

### Minimizing regulatory burdens

Later this year, CALGB and NCI will initiate pilot testing of a central IRB. NCI will convene an IRB organized according to OPRR guidelines. All CALGB protocols will be reviewed by the central IRB and the IRB comments and approval notification will be distributed to those CALGB institutions that participate in the pilot program. Local IRBs

will have the option of accepting the review/approval of the central IRB in lieu of their own review of the protocol.

### Enhancing communication within and between groups

Later this Spring, CALGB will begin on-line patient registration to selected protocols. During the summer of 1999, we anticipate discontinuing monthly protocol mailings as all recent CALGB protocols and forms will be available at our re-designed web site. This will eliminate the need for affiliates to rely on main member institutions to receive new protocols for activation. Last Fall, all CALGB CCOPs and selected affiliates received approval to register patients directly with CALGB, without having to go through a main member institution. All of these changes will facilitate more rapid communication between CALGB and our network of main member and affiliate institutions. In addition, CALGB continues its data reduction efforts and all of the cooperative groups are collaborating in a re-design of forms to simplify data acquisition across inter-group studies.

### Increasing industry collaboration

CALGB continues to enjoy outstanding collaborations with the pharmaceutical industry. Our studies have, and will continue to, form the basis for FDA approval of new oncology drugs or new indications for older drugs. Our colleagues in the pharmaceutical industry remain eager to work with us to introduce the most exciting new agents into cooperative group studies. The Coalition of National Cancer Cooperative Groups, of which CALGB is a founding member, is also becoming a powerful force in reaching out to both the pharmaceutical and insurance industries. A recent important initiative culminated in the announcement by United Healthcare of their willingness to support patient care costs for patients enrolled on clinical trials developed by Coalition members and an ongoing negotiation will permit the Coalition members to participate in an international study conducted by Rhone Poulenc Rorer in patients with metastatic gastric cancer.

### Paying for work performed

Last Fall, Dr. Klausner informed the cooperative group chairs that fiscal year 1999 will bring a substantial increase in the NCI budget. Recently we learned that the cooperative group budget will be increased by approximately \$22 million compared with last year. Although the precise budget allocated for CALGB has not yet been determined, we anticipate that increased funds will be available to fully support the Statistical Center and to compensate affiliate institutions at a substantially higher rate than previously for accrual to treatment studies.

These considerable changes are sure to challenge us in many ways as we move toward the next century of cooperative group research. I have no doubt, however, that CALGB will continue to play a leading role in improving the lives of patients with cancer in the new millennium.

# CALGB GROUP NEWS

## COMMITTEE NEWS

### New Transplant Committee Chair

Charles Linker, M.D., University of California at San Francisco, took over as chairman of the Transplant Committee Feb. 1, 1999, replacing David Hurd, M.D. Linker, 51, has served on the CALGB Leukemia Committee since 1991, and is currently the director of the Adult Leukemia and Bone Marrow Transplant Program at UCSF. Linker joined UCSF in 1978 after completing his medical degree, internship and residencies at Stanford. He has been active in leadership committees in ASCO and ASH and the Leukemia Society of America. Hurd will continue his active involvement in CALGB as Principal Investigator at Wake Forest.

### Lymphoma Committee Leadership Changes

George Canellos, M.D., Dana Farber Cancer Institute, accepted appointment as Chair of the CALGB Lymphoma Committee. Canellos was the Lymphoma Committee vice chair and had taken on the role of acting Chair after the departure of Dan L. Longo, M.D. The new Lymphoma Committee vice chair is Andrew Zelenetz, M.D., Ph.D. of Memorial Sloan-Kettering Cancer Center, New York.

### GI Committee Study to Go International

CALGB 9581, a phase III adjuvant study of monoclonal antibody 17-1a immunotherapy for colon cancer, will be opened for accrual in the United Kingdom in March 1999. QUASAR, a multi-center cancer clinical trials group in the U.K. representing 200 institutions with over 1000 investigators, expressed a strong interest in participating in this intergroup GI trial. QUASAR stands for Quick And Simple And Reliable. This trial will be the first multinational study that CALGB has undertaken. CALGB Chair Richard Schilsky stated that this international collaboration not only bodes well for the success of CALGB 9581, but also serves as an important step in allowing CALGB to develop and implement the necessary infrastructure to do more international clinical trials in the future.

## CALGB MEMBER NEWS

### New Principal Investigators at Walter Reed and Wake Forest

John C. Byrd, M.D. and David Hurd, M.D. are new CALGB PIs at Walter Reed Army Medical Center and Wake Forest University School of Medicine, respectively. Hurd replaces Dr. M. Robert Cooper at Wake Forest. Dr. Hurd has been active in CALGB leadership for 20 years. He

recently stepped down as chairman of the Transplant Committee to devote more time to these new responsibilities. Byrd, a CALGB member since 1995, serves on both the Leukemia and Correlative Sciences committees. He replaces Nancy A. Dawson, M.D. as Walter Reed PI.

### CALGB Welcomes Two CCOPs

The Illinois Oncology Research Association (IORA) CCOP and the Cancer Centers of the Carolinas-Greenville CCOP have joined the CALGB as part of the NCI Division of Cancer Prevention CCOP pilot program. Both CCOPs chose the CALGB as their second multi-disciplinary cooperative group affiliation. The IORA's primary research base is the NCCTG; Greenville CCOP is affiliated with SWOG.

IORA is a network of 20 hospitals, 2 radiation facilities and a hematology/oncology private practice in central Illinois. Fifteen investigators affiliated with IORA will participate in CALGB studies. The Responsible Investigator is John W. Kugler, M.D. IORA accrues approximately 150 patients annually to treatment studies and 75 to 100 patients to cancer control studies.

Greenville CCOP is a South Carolina community-based hematology/oncology physician practice with 10 clinical investigators. It accrues from 75-100 patients to treatment studies per year, and 50-75 patients to cancer control studies. The Principal Investigator is Jeffrey K. Giguere, M.D.

## MEETING NEWS

### Fall Group Meeting Attendance Up

Nearly 700 CALGB members and colleagues attended the Fall Group meeting in New Orleans in November, 15% higher than expected, according to CALGB meetings manager Helen Pollard. The plenary session focused on Cancer in the Elderly (*see articles beginning on page 6*). The Fall Group meeting included a sold-out workshop on the role of genetics in clinical cancer research and the first meeting of the new Patient Issues Committee.

### Summer Group Meeting in Toronto

The CALGB 1999 Summer Group meeting will be held in Toronto, Ontario, at the Sheraton Centre Hotel, June 25-27, 1999. Detailed meeting information and registration forms will be included in the spring newsletter, sent in late April. Registration forms will be available on-line at the CALGB web site by April 15. ([www-calgb.uchicago.edu](http://www-calgb.uchicago.edu)). The Central Office requests that members wishing to register early watch the web site for meeting announcements or wait for meeting information to arrive in the spring *CAL•GAB* Newsletter.

The *CAL•GAB* is published quarterly by the Cancer and Leukemia Group B and is distributed free to the CALGB active membership. Suggestions for articles are encouraged. The next copy deadline is March 30, for the Spring 1999 edition.

Articles and correspondence should be sent to:  
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# Changes to Cooperative Group Clinical Trials Impact CALGB

*Overview continued from page 1*

## **Increase the pool of certified investigators participating in clinical trials.**

The NCI's Expanded Participation Project, a program to expand participation of oncologists who are not currently in cooperative groups, opened in the fall of 1998. For this pilot project, the NCI selected non-affiliated organizations that will be able to enroll patients on six existing cooperative group protocols—four of which are CALGB studies.

## **NCI CCOP Program to expand the portfolio of protocols available to CCOPs**

The NCI has entered 14 CCOPs in a national pilot trial which allows them to participate in protocols from a second multi-disciplinary cooperative group. CCOPs are currently allowed to be members of up to 5 cooperative groups, but only one of those can be a multidisciplinary group, such as CALGB, ECOG, SWOG, or NCCTG. Two CCOPs participating in the pilot program have joined CALGB as a result, and will be able to enroll patients on all CALGB studies.

## **CALGB CCOPs test open enrollment to SWOG studies**

Simultaneously, CALGB and SWOG are testing a program of opening accrual to SWOG studies directly to CALGB CCOPs. Only SWOG studies in diseases and disciplines not covered by CALGB studies will be available to CCOPs. *(See story below)*

## **Centralized IRB Trial**

The CALGB will pilot test a national Institutional Review Board to review Cooperative Group protocols. Local IRBs can expedite or bypass local review by relying on the protocol reviews of the centralized IRB. *(See story below)*

## **National network of accruers to clinical trials**

A common theme of many of these programs is opening clinical trials to a national network of cooperative groups and cancer investigators. Cooperative group institutions will have a broader portfolio of studies on which to enroll patients. While cooperative groups would continue to develop innovative research concepts and conduct their own studies, there may be fewer separate phase III trials investigating similar treatments: the NCI cooperative groups will collaborate more on determining which research concepts will become national clinical trials, open to accrual across all cooperative groups.

Many of these programs will be tested for two or three years, beginning in 1999, during which time the NCI, CALGB and other cooperative groups will gain experience in resolving the logistical and administrative issues that arise, and determine which initiatives are worth pursuing.

## **CALGB CCOPs TO OPEN SELECT SWOG STUDIES**

CALGB CCOP institutions will be allowed to participate in a limited set of Southwest Oncology Group protocols in a pilot project opened this year. SWOG studies in disease areas not covered by CALGB disease committees have been made available to members of the ten current CALGB CCOP networks.

SWOG committees have active treatment studies for diseases such as head and neck cancers, brain tumors, gynecological malignancies and sarcoma, not available within CALGB.

Ten SWOG protocols in those disease areas have been selected to date and will be opened up to CALGB CCOPs. In those instances the CALGB CCOPs will function as SWOG institutions. They will work directly with SWOG to enroll patients and channel data to the SWOG data management center. CALGB CCOP members are automatically eligible and do not need to apply to participate in this program. Training in SWOG data procedures and use of SWOG forms was offered at the Fall Group meeting to CALGB CRAs.

The one-year pilot project will assess the value of opening SWOG studies in disciplines that CALGB does not study to other CALGB institutions.

## **CALGB CENTRALIZED IRB PILOT PROGRAM**

To streamline implementation of new clinical trials, the NCI's Clinical Trials Monitoring Branch has invited CALGB to pilot test a centralized Institutional Review Board. The NCI worked closely with the Office of Protection from Research Risks to develop this pilot project. The NCI will establish a central IRB to review all protocols submitted to CTEP by CALGB; local IRBs at a select group of CALGB institutions can opt to expedite local review by relying on the central IRB's protocol review.

The centralized IRB could increase patient access to clinical trials as well as shorten the length of time it takes to complete trials and report results. Eliminating duplicative efforts by each local IRB can reduce the overall review and approval time for new protocols, allowing patient accrual to start sooner.

In this test the central IRB will also process and analyze all adverse event reports on the protocols it has reviewed, and forward relevant findings to each participating local IRB.

Twenty to thirty CALGB institutions will be selected to participate—representing academic medical centers, community hospitals, CCOPs and private practices. This pilot project will be coordinated at the NCI by a new Human

*Centralized IRB trial continued on page 5*

# Clinical Trials Implementation Committee Recommends Changes to National Clinical Trials Program

The initial pilot projects testing potential improvements to the current clinical trials system stem from the recommendations of the NCI's Clinical Trials Implementation Committee, of which CALGB Chair Richard Schilsky and GI Committee Chair Robert Mayer were members. The goals of the committee were to promote the best scientific opportunities, encourage high-risk novel ideas, and to establish means to support the best trials and the best science with funding and administrative resources.

Increasing accrual and patient access to protocols is seen as essential to improving the clinical trials process. The program will work towards having an open menu of protocols across the country, facilitating cross-group patient registration. Clinical trials of new therapies should be an available option to all cancer patients, and the long-term goal is that all NCI-qualified oncologists and physicians who are capable of enrolling patients in clinical trials will be able to do so.

The key elements of the program are as follows:

- **State of the Science Meetings**

Multidisciplinary groups of investigators will convene in regular national forums to frame the key research questions in each disease area. These meetings will be used to identify research opportunities and information gaps in current science, and to share these directives with the broader research community. State of the Science meetings will replace the current CTEP strategy meetings.

- **Empower Idea Generators**

Instill an open, competitive environment to foster innovative concept development by a wider range of researchers and investigators. Researchers from existing Cooperative Groups, cancer centers, community and private practices, and industry will be encouraged to bring concepts forward for potential development into national clinical trial protocols. CALGB investigators should continue to use the CALGB disease/modality committees and committee chairs as conduits for research concepts.

- **Protocol concepts reviewed by national disease-specific peer review committees to speed up review and approval of new concepts.**

New peer review committees will be formed later this

year to replace the current NCI CTEP review for new concepts in GU and lung cancer. Each 15-member committee will be composed of representatives from Cooperative Groups, the NCI and other types of cancer research organizations, such as cancer centers and SPORES.

These committees will be charged with providing fast-response real-time review of concepts. Concepts ranked in the excellent to outstanding range could then be activated nationally, available to all cooperative groups.

If this concept review method proves successful in GU and lung cancer, concept peer review committees in other major disease areas will also be created.

- **Cooperative Groups retain primary roles**

Concepts for new protocols must be attached to an NCI-funded statistical center capable of managing the data collection and analysis of a proposed trial. (*NCI increases funding to cooperative group statistical centers to full peer-recommended levels—see Message from the Chair, page 2*). The cooperative group which initiates an approved protocol concept will produce the final protocol document with the NCI. The conduct of the study, analysis and publication of results will remain the responsibility of the sponsoring group.

- **Cross-group open enrollment facilitated by new Clinical Trial Support Units (CTSUs) for patient registration and administrative support**

New administrative entities will be created to register patients and offer administrative support to institutions outside of the protocol-sponsoring cooperative group. The CTSUs will manage protocol distribution, randomization, data submission, training of investigators and CRAs, and other tasks that would otherwise need to be repeated across every cooperative group participating in the open protocol. Institutions belonging to the sponsoring cooperative group will continue to register patients directly, while other institutions will work with the appropriate CTSU for patient registration and data transmission.

These CTSUs will first be created to support new studies in respiratory and GU cancers.

## CALGB CENTRALIZED IRB PILOT PROGRAM *continued from page 4*

Subject Protection Review Board (HSPRB). The new HSPRB administrator will work with the CALGB to select participating institutions and establish review and operating procedures.

The pilot project is expected to last two years. The NCI's goal is to determine the value and acceptance of an ongoing central IRB for multi-center trials for all cooperative groups.

If you are a CALGB Principal Investigator or a Responsible Investigator, please contact the CALGB

Central Office by March 31, 1999 if you are interested in having your institutions participate in this pilot project. It is important that we have a good selection of the various types of institutions that participate in the CALGB: we will need academic, community and CCOP institutions as well as physician groups.

Contact: **Rene Cristwell, Regulatory Affairs Coordinator**

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## FALL MEETING SCIENTIFIC SESSIONS

### Cancer in an Aging America

*Rosemary Yancik, Ph.D., National Institute on Aging*

Aging is a high risk factor for cancer. Patients 65 years and older account for 60% of all newly-diagnosed malignancies and 70% of cancer mortality in the United States. Older Americans are eleven times more likely to be diagnosed with cancer than individuals under 65. The age-adjusted incidence rate for persons 65 years and older is 2261.0 per 100,000 as compared to 207.3 for individuals under aged 65, a dramatic difference.<sup>1</sup> As the older-age segment of the U.S. population continues to expand in absolute numbers as well in proportion of the total population, there will be many more cancer patients in the first part of the next century, assuming incidence rates remain the same.

Several major tumors with high incidence rates disproportionately affect the older population. Eleven major malignancies accounted for 73% of cancer cases registered by the NCI Surveillance, Epidemiology and End Results (SEER) program from 1991 to 1995—and two-thirds of these patients were over 65. Clearly, older Americans bear a great burden of cancer incidence. Yet persons in the 65+ age segment of the population, those most vulnerable to cancer, have not received a fair share of cancer treatment research efforts. Cancer clinical trials research has not addressed many crucial issues involved in treating older patients. Older men and women who are diagnosed with cancer are already burdened by age-related declines in function, physical impairment, and concurrent diseases. Data on tolerance and response to adjuvant therapy or multimodality treatment regimens are urgently needed (controlling for age-associated conditions, i.e. alterations in physiologic parameters and therapeutic risks to the cardiovascular, pulmonary, and renal systems).

To stimulate NIA/NCI financial support for cancer clinical trials research on clinical trials involving older persons, a National Institute on Aging (NIA)/NCI initiative was announced this fall to support competitive applications from by NCI-sponsored Clinical Cooperative Groups, including the CALGB. The initiative encourages: (1) expansion of accrual of older patients through development of new trials and/or modification of existing clinical trials; (2) analysis of data from existing large-scale trials, or pilot studies, to study issues relevant to older-aged patients; (3) age-relevant correlative science studies; and (4) ancillary studies that address age-related scientific questions about the epidemiology, genetics, and pathology of cancer. The objectives are to produce new treatment strategies for older-aged cancer patients and a body of much-needed information about cancer in the elderly that can be disseminated to the medical practice community-at-large.

An NIA/NCI partnership offers an innovative way for the NIA to support research on cancer in older patients via the

NCI clinical trials infrastructure and its peer review process. The NIA will commit up to \$2.5 million per year for up to five years to fund six to ten projects, via the U10 grant mechanism, from NCI Cooperative Groups responding to this solicitation.

#### Research Objectives

Malignancies emphasized for the NIA/NCI research initiative are cancers of the breast, colon, rectum, prostate, pancreas, lung, bladder, stomach, non-Hodgkin's lymphomas, head and neck, and ovary. Research areas include, but are not limited to:

- Dose adjustment for antineoplastic agents and/or radiation therapy in the presence of comorbidity, intercurrent disease, and age-related physiologic changes;
- Age-related tolerance or increased toxicity to specific drugs;
- Comorbidity and intercurrent diseases as they may affect treatment and survival outcome;
- Prognostic aspects of dose intensity, cumulative dosage of chemotherapy, and/or radiation therapy;
- Minority/ethnicity survival advantages and disadvantages as linked with heterogeneity of the aged host and tumor characteristics;
- Age-related differences in patterns of invasion, metastasis, and disease progression;
- Methods to evaluate functional status of elderly patients to identify significant impairments that will influence therapeutic regimens;
- Elucidation of basic biologic endpoints, including those of immediate clinical relevance (e.g., pharmacokinetics, hematopoietic stem cell/differentiation capacity);
- For site-specific protocols, companion prospective studies of patients 65+ inadmissible to protocol (e.g., patient group comparisons on comorbidity, physical, and physiologic functioning).

#### Research Needs

An integration of aging and cancer research will address crucial questions. What is known in oncology and geriatric medicine must be applied on behalf of older persons. The challenge of the imbalance of cancers striking those in the older age strata of the population is before us. The NIA/NCI clinical trials research initiative will enhance the development of a body of evidence to guide treatment of cancer in the elderly. It is gratifying to witness the changing climate regarding research on cancer in the elderly. More and more resources are now being targeted at identifying and solving the complex problems of treating older cancer patients.

#### References:

1. Ries LAG, Kosary CL, Hankey BF, Miller BA, Edwards BK (Eds). SEER Cancer Statistics Review, 1973-1995, National Cancer Institute, Bethesda, MD, 1998

# Competing Risks and Their Impact on Survival Analyses

*Bercedis Peterson, Ph.D.*

*CALGB Statistical Center*

Among the important endpoints used in clinical trials in oncology to judge the success of a therapy are various "time-to-event" outcomes. These outcomes include, for example, time-to-death (overall survival), time-to-progression, and time-to-response. Breast and prostate protocols often measure success by time-to-local recurrence; myelodysplasia protocols may measure success by time-to-transformation to AML. The Kaplan-Meier method is commonly used to describe these time-to-event distributions (also called survival distributions). This method produces a graphical display of the survival distribution and allows the calculation of some important descriptive statistics, for example, the median survival time and the probability of survival to 6 months, to 2 years, or to whatever time point is of most interest.

The appeal of the Kaplan-Meier method is that it permits the calculation of these distributions and statistics even though many patients may not yet have experienced the event of interest at the time of the analysis. Such patients are called "censored." In fact, there would be no need to use the Kaplan-Meier method to calculate, say, the probability of surviving to 2 years if every single patient had died by the time of the analysis. We would simply estimate this probability by dividing the number of deaths at 2 years by the total sample size.

In the calculation of Kaplan-Meier curves both statisticians and clinicians have been tempted to "censor" patients for reasons other than the fact that they simply had not yet experienced the event by the time of the analysis. For example, in an analysis of time-to-transformation to AML, there is temptation to (incorrectly) censor patients who die before transforming. In an analysis of time-to-local failure, it is quite common (and incorrect) to censor patients who first experienced distant failure. In this latter example distant failure "competes" with local failure for the lives of the patients. In the former example, death competes with transformation-to-AML. Consequently, the terminology "competing risks" is often used to explain why it is incorrect to censor patients in these and many other contexts.

For example, competing risk terminology can be used to explain why it is incorrect to censor "other" deaths in an analysis of overall survival. In particular, we say that the lives of patients are competed for by a cancer-related force of mortality and by an other-death-related force of mortality, and these two forces are not independent. That is, a patient pulled strongly by one force is more likely to be pulled strongly by the other. One could argue, for example, that a patient at high risk of a disease-related death is probably also at higher risk of suicide, of death by careless

accident, or death by heart failure. By censoring "other" deaths, these higher-risk patients are treated exactly like the lesser-risk patients who are still alive. This makes the survival curve look better than it really should. Analogous arguments apply to other competing risk situations, and in most cases the result of incorrect censoring is that the Kaplan-Meier curve will look higher than it should. Thus, the median survival time and probabilities of surviving to various time points will be overly optimistic.

An important example of incorrect censoring that is a bit different from the ones covered above is the censoring at the time of a bone marrow transplant in an analysis of overall survival. This situation is unique because BMT may be used for both poor prognosis and good prognosis patients. In all the other examples above the censoring event indicated poor prognosis.

There is no elegant solution to the problem of competing risks, and it is not the intent of this short article to review the solutions that have been proposed. The interested reader is referred to an excellent article by Gelman et al. published in *JCO*, vol. 8, 1990, pp. 548-555.

## Lymphoma in the Elderly

*Stuart M. Lichtman, M.D.*

*Don Monti Division of Medical Oncology, Department of Medicine, North Shore University Hospital-New York University School of Medicine, Manhasset, New York*

Persons 65 years of age and older are the fastest growing segment of the United States population. SEER data shows there will be a dramatic increase in the number of elderly patients with non-Hodgkin's lymphoma. In 1986, a review by the Southwest Oncology Group showed that older age carries a worse prognosis and that arbitrary initial dose reductions in chemotherapy may have contributed to the poor outcome. In 1988 the University of Nebraska reported that differences in survival between younger and older patients were due to other causes of death not obviously related to the lymphoma or its therapy. In 1993 an intergroup randomized trial established CHOP as the standard therapy. The International Non-Hodgkin's Lymphoma Prognostic Factors Project demonstrated that the clinical characteristics of patients over 60 years of age were comparable with those younger. Based on five clinical factors, an International Prognostic Index was developed which is able to predict complete response and 5-year survival. The CR rates for older and younger patients were similar, but the older patients were much less likely to maintain their CRs. This resulted in an age-related difference in survival.

There have been four randomized trials in older patients with advanced, aggressive lymphoma. Sonneveld compared CNOP to CHOP using an every four week regimen. The CHOP regimen was superior in response (CR 49% v. 31%), but overall survival was equivalent. Toxicity was similar and CHOP was tolerated by the majority of elderly

patients. Bastion, et al. demonstrated that anthracyclines were crucial to good outcome in the older patient population in a study comparing CVP and CTVP (T=THP-doxorubicin; pirarubicin). Meyer studied CHOP in weekly 1/3rd divided doses vs. standard CHOP. There was no difference in response or survival and the standard regimen was preferred. Tirelli performed a randomized trial of CHOP vs. VMP (etoposide, mitoxantrone, prednimustine). This study showed superiority of the CHOP regimen in both complete response rate (45% v. 27%) and two year progression free survival (55% v. 25%). Therefore, CHOP should be the standard for good performance status older patients. These studies confirmed that 25% of patient deaths were due to non-lymphoma causes.

Alternative regimens are needed, particularly for those patients with significant comorbidity and frailty. Many non-randomized clinical trials using different drugs to reduce toxicity have been performed. Mitoxantrone has been used to minimize cardiac toxicity, nausea, vomiting, mucositis, and alopecia. Oral etoposide and prednimustine have also been incorporated. Comparisons between trials are limited due to differing entry requirements and demographics. The 2-year disease-free survival rate ranges from 15% to 55%. These treatment modifications may have compromised efficacy. However, they do fulfill the need of an alternative regimen for selected poor performance status patients.

It is usually inappropriate to pursue aggressive therapy in older patients with relapsed/refractory disease, particularly bone marrow transplantation. However, there are data to show that well selected older patients can tolerate and may benefit from the procedure. Careful patient selection and evaluation are crucial. Interpretation of transplant data in the older patient must take into account this selection process. Nonmyeloablative or "transplant-lite" studies may be applicable to older patients due to their lessened toxicity.

Older patients are at increased risk for anthracycline cardiotoxicity. Pre-existing cardiac disease and hypertension also appear to be risk factors. There are a number of doxorubicin substitutes approved including epirubicin, mitoxantrone, idarubicin, and liposomal compounds. The equitoxic and/or equieffective dose to doxorubicin is still not standardized. Anthracycline toxicity may be lessened by prolonged infusions or low-dose weekly schedules and protectors.

Less toxic, non-myelosuppressive therapy such as rituximab, radioimmunotherapy and interferons may prove valuable. Issues for future study include clinical trial design, assessment of performance with geriatric functional scales, polypharmacy, comorbidity, insurance, transportation and social support.

## ONCOLOGY NURSING

# Management of Patients with Melanoma

*Mary Elshamy, ARNP, AOCN, Norris Cotton Cancer Center, Dartmouth Hitchcock Medical Center, Lebanon, NH*

### **Melanoma: what is this cancer?**

Melanoma is a potentially deadly skin cancer that occurs from a transformation of melanocytes to malignant cells. This may or may not occur in a nevus (mole). Prognosis correlates with depth of invasion into the layers of the skin. The 10-year survival for a thin melanoma is over 95% while less than 50% of patients with deeper melanomas live 10 years. Measurement is defined as Clark level, histologically described skin layers, or Breslow depth which measures invasion in millimeters. In the United States the incidence of melanoma is rising exponentially. It is estimated that in 1998 there will be 41,600 new cases diagnosed and 7,300 deaths from melanoma. By the year 2000 the lifetime risk for melanoma is predicted to be one in 75.

### **Prevention**

Prevention of melanoma is key to reducing the mortality from this cancer. It is believed that sunlight is involved in melanoma risk, but the exact relationship of sun exposure to risk is not entirely clear. Sun exposure by 'at-risk' people is the only environmental factor that is consistently linked. 'At-risk' people account for only 30-50% of those who develop melanoma. Risk includes fair complexions that burn or blister easily, blonde or red hair, and blue, green or grey eyes. Excessive sun exposure in childhood may identify people at risk. A family history of melanoma and dysplastic nevi (atypical moles) and a large number of moles, >100 on an adult or >50 if under age 20 can predict a risk of melanoma of nearly 100%.

Reducing sun exposure is an important strategy for preventing melanoma. Everyone should avoid mid-day exposure to the sun, wear hats with broad brims, cover with tight-weave dark clothing, place canopies close to the ground and use adequate and frequent applications of sunscreen with an SPF of 15 or greater to reduce exposure. Behavioral scientists recommend that promoting habitual behaviors is more effective than adjusting behaviors according to the weather. The risk of burns is greater at intermediate temperatures and when there is cloud cover. Thus, education of the public is most effective when the habit of protection from the sun is reinforced. In other words, use sunscreen routinely not adjusting for the weather, just like wearing a seat belt whenever in the car, not just when the traffic is heavy!

### **Early Detection: ABCD rules**

Skin examination is an important early detection tool for melanoma control. This includes frequent and thorough skin exams using a partner and/or a mirror to examine all parts of the body. Those parts of the body that are difficult

to see are often areas where melanomas are hiding. Identifying a melanoma lesion is made easier by following the ABCD rules.

**A=asymmetry** with half of the lesion looking different from the other half

**B=border** of the lesions may be irregular and scalloped in appearance

**C=color** of the lesion may be black, blue, red, brown or tan and **changing**

**D=Diameter** of the lesion is changing and growing, often greater than 4mm

Frequently nurses who care for patients with melanoma hear that the lesion arose without any of these typical warning signs, which can be frightening and frustrating for patients. However teaching surveillance is an important way to raise awareness among the public and promote consumer demand for protection from a deadly illness.

### Staging of melanoma

The stage of melanoma is defined by the depth of the lesion into the skin and the spread of cells to lymph nodes and organs. Surgery is the primary intervention for treatment of melanoma stages I-III and may be useful in stage IV disease. Patients are often treated using a multidisciplinary approach including dermatologists, plastic and general surgeons, oncologists and nurses at all levels of intervention. Patient education is important at all stages of disease and a critical role for the nurse.

### Treatment toxicities

Patients undergoing treatment of melanoma often experience profound adverse events that occur over long treatment periods. The most common toxicities associated with biologic therapy are flu-like symptoms that range from mild fevers and myalgias to high fevers, rigors, dehydration, arthralgia, headache, insomnia, depression and confusion. Combination therapies compound the associated toxicities and add to the flu-like distress, vaccines can cause injection site reactions while chemotherapy agents add hematopoietic toxicities along with nausea, vomiting, neurologic changes and others. The patient undergoing treatment for melanoma, whether adjuvant treatment for stage II or III disease or aggressive therapy for disseminated disease, will experience many symptoms related to their therapy. Expert nursing intervention, support and patient education are critical for maintaining the patient through treatment.

### Melanoma Working Group at CALGB

Nurses will be challenged by the Melanoma Working Group to manage patients who undergo novel research approaches to treating melanoma. Patients with Stage I, II and III disease will be recruited to participate in research and will be the principal patient population to be studied by this cooperative group. The ability of patients to stay on treatment and remain in a clinical trial will be strongly influenced by their nurses' skill with symptom management.

## MELANOMA STAGING:

### STAGE IA:

Tumor depth:  $\leq 0.75$ mm

Treatment: surgery with surveillance

5-year survival: 90-98%

### STAGE IB:

Tumor depth:  $> 0.75$ mm and  $< 1.5$ mm

Treatment: surgery with surveillance

5-year survival: 70-95%

### STAGE IIA:

Tumor depth:  $> 1.5$ mm and  $< 4$ mm,  
negative regional (sentinel) lymph nodes

Treatment: surgery

Clinical research testing: interferon alpha 2a and others

5-year survival: 60-80%

### STAGE IIB:

Tumor depth:  $> 4$ mm,  
negative regional (sentinel) lymph nodes

Treatment: surgery, high dose interferon alpha 2b

Clinical research testing: varying schedules and formulations of interferon, vaccines, gene therapy, chemotherapy and combinations of biologic agents

5-year survival: 40-50%

### STAGE III:

Tumor depth:  $> 4$  mm and/or positive regional lymph nodes

Treatment: surgery, lymph node dissection, high dose interferon alpha 2b

Clinical research testing: varying schedules and formulations of interferon, vaccines, gene therapy, chemotherapy and combinations of biologic agents

5-year survival: 30-40%

### STAGE IV:

Any tumor depth, any positive lymph node, distant metastases

Treatment: surgery for palliation or excision of tumor for autologous vaccine, high dose interleukin-2, interferon with interleukin-2, chemotherapy, biochemotherapy, radiation therapy, investigational therapies including novel combinations of agents, vaccines, gene therapy

5-year survival:  $< 10\%$

## OPERATIONS, DATA MANAGEMENT, INFO SYSTEMS

### CTEP Implements New Data Update System

*Michael F. Moloney, Director, CALGB Information Systems*

All cancer clinical trials approved after March 5, 1998 by the Cancer Therapy Evaluation Program (CTEP) are required to be reported to CTEP using the Clinical Data Update System.

CDUS is the primary clinical trial data resource for the NCI's Division of Cancer Treatment and Diagnosis (DCTD) and the Division of Cancer Prevention (DCP). It is based on new cumulative quarterly electronic reports supplied by clinical trials groups and non-groups. These reports replace all previous CTEP monitoring mechanisms, and contain data required to meet the scientific, regulatory and administrative needs of the NCI. The CALGB Information Systems group at the Statistical Center, Duke University, generates and submits CDUS reports for CALGB. CDUS adheres to the International Committee on Harmonization (ICH) coding standards, which uses the International Medical Terminology (IMT) dictionary for reporting disease classification, adverse events and other study-related activities and events. More information on the ICH can be found at the web site <http://www.ich.org/>.

#### Which trials are reported to CDUS?

A CDU report is required for all DCTD- and DCP-sponsored Cooperative Group and CCOP Research Base trials (Phase I, II and III), including:

- all treatment trials using DCTD-supplied investigational agents or non-NCI agents (commercial or investigational)
- all non-treatment trials involving 100 or more patients and all CCOP cancer prevention and control trials

#### CDUS Report Types

There are two types of CDUS reports: abbreviated and complete. The characteristics of the trial determine which CDUS report type will be used. The abbreviated data set is limited to protocol administrative information and patient demographics. The complete data set also includes administrative patient information (e.g., registering institution code, patient treatment status), treatment information (e.g., agent administered, total dose per course), adverse event (toxicity) information (e.g., toxicity type, grade), and response information (e.g., response observed, date response observed).

#### How does CDUS affect CALGB participants?

If a trial is to be reported under CDUS specifications, data forms must be designed to collect the information required.

Members of the study team (study chair, co-chairs, statisticians, protocol editor, data coordinator) must check the CDUS guidelines to be certain that appropriate data are retrieved.

CALGB CRAs should be aware that the mechanisms and conventions to collect patient-specific treatment-related information are changing to reflect the CDUS requirements.

#### How do I know if a trial must be reported using CDUS?

CTEP informs the CALGB protocol editor if CDUS reporting is required and indicates the type of report to be submitted. The protocol editor updates the CALGB central database and also informs the study team of the CDUS report type required, if any, for the trial.

More information about CDUS and CTEP Informatics is available at <http://ctep.info.nih.gov/>; complete CDUS specifications are at <http://ctep.info.nih.gov/ctepinformatics/cdus/default.htm>.

### CALGB Reduces Data Collection

*Debbie Sawyer, Director, CALGB Data Operations*

An ad hoc CALGB Data Reduction Committee was created in Fall of 1997. It was charged with:

- assessing the amount, frequency, format and process of data collection for CALGB phase III protocols;
- reducing overall data collection in a way that meets, but does not exceed, the stated objectives of a study.

The committee was jointly chaired by Dr. David Grinblatt, CALGB Executive Officer, and Debbie Sawyer, Director of Data Operations. Committee members included: Institutional Investigator Dr. Antonius Miller, CCOP Principal Investigator Dr. James Atkins, CRA Committee Representatives Barbara Barrett and Jean Roark, Nursing Committee Representative Deborah Berg, Statistician Donna Hollis and DMC Representatives Sherry Breaux, Michael Leonard, Michael Moloney and Rick Preston.

The committee presented 12 data reduction recommendations. All were approved by the Executive Committee, and implementation is either in progress or has been completed:

#### 1. Eliminate flow sheets from all phase II and III trials.

Flow sheets require a major expenditure of time by CRAs, oncology nurses and DMC staff, but have a minor impact on toxicity reporting and a very minimal impact on the primary objectives of phase II and III trials. The committee encouraged the elimination of flow sheets, but emphasized that it must be accompanied by the creation of well-designed coded forms, which ensure complete data capture. The committee also recommended that grade 3 or greater toxicities should be described on an addendum flow sheet. Implementation of this policy began on a study-by-study basis in Spring 1998, and effective June 1998, flow sheets were dropped from all new phase III protocols. Elimination of flow sheets on future phase II studies will be determined on a study-by-study basis.

#### 2. Delete laboratory tests deemed unessential to answering the objectives of a trial.

Some tests which are appropriate for monitoring patients during treatment in phase I and many phase II trials are not necessary in phase III trials (especially if the trial involves well-tested regimens of therapy). Because requiring these tests often leads to costly "overtesting," it was recommended that follow-up lab tests to assess toxicities should be listed as "prn." Those tests which are required to assess the need for dose adjustments on Day 1 of each cycle should still be included.

#### 3. Delete the requirement for differentials as part of the CBC unless the WBC is below 3000, and allow machine differential (except on leukemia studies).

Some committee members reported that several institutions had encountered significant difficulties mandating manual differential counts. The Data Audit Committee was instructed to allow machine differentials. Protocol Editors were advised that differentials would no longer be required as part of the CBC in new protocols.

#### 4. Educate Study Chairs on the need to keep required laboratory and staging tests to the minimum necessary to meet the objectives of the study.

This directive was presented at the Study Chair Workshop in June 1998

5. **Eliminate 4-week confirmation scanning and testing unless assessing the duration of remission is the primary objective of the study.** This mandate has been implemented on all new protocols.
6. **Revise the content of CALGB forms to ensure that it is study-specific and mirrors the study objectives; link format and submission to protocol-defined evaluation schedules (Case Report Format).** The Committee felt that the forms-development process could be simplified by incorporating disease-specific modules which could be supplemented with study-specific data points. A committee headed by Michael Leonard was appointed to evaluate software packages to be used for forms development. The new format is being used on CALGB 9732 and will allow the Group to pilot this approach.
7. **Eliminate unnecessary data items from generic forms.** A committee headed by Sue Budinger was appointed to evaluate generic forms. This committee revised forms C-113, C-215, C-300 and C-400. New versions of C-113, C-215 and C-300 have been implemented. Implementation of form C-400 is pending.
8. **Discontinue the submission of the Patient Background Form on all protocols where it is not required to fulfill a study objective.** The Psycho-oncology Committee reduced the Patient Background Form to one page. The prior version will be used to collect relevant information for on-going studies. The Executive Committee ruled that Study Chairs have the option to decide whether the Patient Background Form is required on new studies.
9. **Develop a one-page study-specific form for each protocol to accommodate the new Common Toxicity Criteria (CTC).** A one-page toxicity form should include no more than 12-15 study-specific expected toxicities. Space will be provided to write in unexpected toxicities with an appropriate prompt for AER submission if the grade warrants an AER. The prevalence and importance of a toxicity will determine its inclusion among the 12 to 15 toxicities listed on a form. For toxicities which have multiple descriptions (e.g., hemorrhage), the most prevalent description will be selected. When choosing between a prevalent toxicity (i.e. alopecia) and a significant toxicity for the study, priority will be given to the more significant toxicity.
10. **Send queries to institutions by e-mail whenever possible.** This recommendation was made by the Data Reduction Committee's CRA and Oncology Nursing representatives. Data Coordinator Dana McDonald polled lead CRAs for their suggestions on e-mail queries. Resulting guidelines state that:
  - Data Coordinators will e-mail the lead CRA directly and copy the contact person if possible;
  - patient identifiers will include the CALGB patient number, patient initials and hospital number;
  - the lead CRA should acknowledge receipt of the request;
  - all responses to the DMC should be routed through the lead CRA.
11. **Make all forms and protocols for active studies available at the CALGB web site by the June 1999 Group meeting.** The Data Management Center has undertaken the task of transferring forms from all active studies to the PDF CALGB web site.
12. **Truncate long-term follow-up for all studies, provided**

**that trial objectives do not require follow-up beyond a specified point.** Long-term follow-up in other settings would be determined by the objectives of the study. All secondary malignancies must continue to be reported. The responsible study Statisticians and Committee Chairs have reviewed all studies to determine the appropriate length of follow-up. Length of follow-up for new studies will be stated in the statistical section of the protocol. The follow-up period for active studies can be determined by accessing the Patient Follow-up Period contained in the Study section of the CALGB IS Client. A list of completed studies for which follow-up is no longer required was distributed in the January 1999 protocol mailing.

## Physician Group Membership Created

The CALGB Board of Directors approved a new type of institutional membership at the Board of Directors Meeting on November 22, 1998. A physician group is defined as a distinct legal entity (with which a services agreement may be negotiated). The investigators in the group must derive their income or compensation from the physician group. It will be treated as an affiliate member of the CALGB, and the same federal regulations that apply to an institution will also apply to a physician group.

If investigators of a physician group are currently members of the CALGB and would like their physician group to become a member of the CALGB, they must:

- Designate an institution with a Multiple Project Assurance (MPA) or Cooperative Project Assurance (CPA) to review protocols for them prior to patients going on study; **or**
- Obtain a CPA for the physician group that will review the protocols.
- If the physician group designates an institution to review their protocols, all investigators must have an Non-institutional Investigator Assurance (NIA) on file at the institution that will review the protocols.
- The physician group must have on file a statement that they will keep track of patients who go on clinical trials.

All previous accrual (prior to 1998) remains with the institution(s) that the investigators in the physician group were previously affiliated with. Audits will be conducted at the physician group office and the physician group will be responsible for obtaining hospital records if the patient was treated at a hospital. The Physician Group will also be responsible for ordering and tracking investigational drugs according to the Investigator's Handbook.

Physicians who are salaried employees of large institutions who do community outreach work are not considered physician groups. If these physicians wish to enroll the patients they see in the community in clinical trials there are other options. The MPA of the large institution may be amended, via discussion with Katherine Duncan, M.D. at the Office of Protection from Research Risks (OPRR), to add the community sites. The Central Office must have documentation on file that the MPA has been amended. The investigators are then able to register patients at the community site via the large institution since the community site then becomes a component of the large institution.

Complete rules and an application packet may be obtained from Rena Cristwell, Regulatory Affairs Coordinator (phone: 773-702-9860 or e-mail: rcristwe@midway.uchicago.edu).

## CALGB Information System Client Software On-Line Access and Patient Registration

*Rick Preston, Analyst/Programmer, Sr.*

Most lead Clinical Research Associates (CRAs) at main member institutions now have access to the CALGB Central Database Server. Selected CCOPs, Central Labs, and some study chairs are also on-line. The Information Systems (IS) Group has developed a Client software application that provides secure access to the Information System computer at the Statistical Center. In July 1997, the Central Office and Statistical Center began using the Client software to update the central database in real-time. After a brief introductory period, the CALGB Operations Committee began to give access to the group membership in preparation for on-line patient registration. The first members to receive the software were lead CRAs at main member institutions. The few lead CRAs who do not yet have access will be on-line as soon as network communications are established by their institutions. The IS Group is working with network specialists at some main member institutions to coordinate on-line access with network firewalls. Once the lead CRAs are on-line, the IS Group will set up accounts for designated backups; then each institution will be contacted one at a time to set up accounts for the remaining CRAs.

The first hands-on database training session using the Client software was held at the Fall Group meeting in New Orleans. Six CRAs volunteered to form a user support committee and conducted an all-day training seminar using the Client software. Members of the committee demonstrated how to use the Client to retrieve information about Groups, Institutions, IRBs, Participants, Committees, and Studies from the CALGB central database. After the demonstrations, the attendees were given a user's guide with a tutorial and assistance was provided with hands-on training. The training sessions will be continued at future Group meetings. Many thanks to the members of the User Support Committee!

Version 2 of the IS Client software will contain the long-awaited On-Line Patient Registration System. It will be available during the first quarter of 1999. CRAs with on-line access and the proper authorization will be able to register patients directly to newly activated studies. Older studies will have to be converted before the new Client software can use them. The system will ask for patient eligibility information specified in the protocol as well as required data for CDUS reporting (see article on CDUS reporting, also in this issue). The Patient Registration System has a Wizard to assist in registering / randomizing a patient to a trial, but it also has a separate patient application to retrieve patient data that a user is authorized to see. As new studies become available to the Client software, the Lab Sample Tracking System (LABTRAK) will also be available for sample submission to the Central Labs. Watch for Version 2 coming soon.

## Quality Assurance of CALGB Administrative Database

*Karen Sartell, Group Administrator*

The Cancer and Leukemia Group B (CALGB) Central Office computerized its institutional, committee, and participant membership, along with its publications and group meeting attendance, in 1990 using FileMaker Pro software. In July 1997, the FileMaker Pro institutional, committee and participant membership data were added to the centralized database for the Group, and were made accessible to the staff at the Central Office and Statistical Center (Biostatistics, Data Operations, and Information Systems) using Client software. For the first time, the Central Office staff could review the studies database and the staff at the Statistical Center had real-time access to the institutions, committees and participants information. In 1998, main member institutions began, one by one, to have access to the Client software. CALGB Community Clinical Oncology Program (CCOP) networks and affiliates that register over 30 patients annually began accessing the Client during the latter part of 1998.

The Central Office staff is working through the transition period following the database conversion, performing quality assurance tasks to verify the accuracy of the administrative database and correcting records where necessary. For instance, duplicate Participant records that were created during the conversion process are being deleted—an on-going project that will be completed in 1999. The Central Office is also working with the Information Systems staff to upgrade quality assurance procedures for entry of administrative data.

The committee list and roster viewed on the CALGB web page are derived from the Group database. We would appreciate it if CALGB participants would take the time to review their records at the web site and let us know if there are any corrections required. If you notice data items that need to be changed, please send an e-mail to [calgb-revisions@uchicago.edu](mailto:calgb-revisions@uchicago.edu). Your written request will be forwarded to the person who is authorized to update the data fields in question.

The Central Office staff is also in the process of performing quality assurance checks on the Studies database. The titles of all active protocols have been reviewed and corrected where necessary. Closed studies are currently under review. This project will continue through 1999.

The Operations Committee, composed of senior leadership from the Central Office and Statistical Center, is developing measurement tools to evaluate various CALGB activities. For example, protocol editors are tracking the development of new protocols with project management software. In addition, the Central Office is reviewing the Implementation Committee Report, that was approved by the National Cancer Institute's Board of Scientific Advisors in September, 1998, and will decide how the CALGB will revise its institutional evaluation to comply with the Implementation Committee Report.

The Central Office will revise the FileMaker Pro publications database in 1999 and add it to the centralized database. Using Client, participants will be able to view the list of publications generated from CALGB studies.

The CALGB is excited about its expanded and accessible centralized database, and welcomes feedback from users of Client software.

## CALGB implements a barcode system for forms tracking

Audrey McKinnon, Lead Data Coordinator

On January 4, 1999, the CALGB Data Management Center (DMC) implemented a barcode system to track data submission forms. For patients registered to CALGB-coordinated studies on or after that date, the system provides preprinted labels that encode study, form and patient information. Data management personnel at each institution are responsible for adding the labels to the appropriate CALGB forms before the data are submitted to the DMC. Upon receipt of data submission forms at the DMC, the information contained in the barcode is scanned into the database. Labels will not be provided for other groups (SWOG, ECOG, etc.) participating in CALGB-coordinated trials at this time. Labels will also not be provided for previously registered patients.

Labels are generated on a daily basis and are mailed weekly from the DMC to CALGB main member institutions for distribution to their affiliates. Ricky Marsh at the DMC ((919) 286-0045, ext. 243) should be contacted if labels are not received for a patient within 3 weeks of registration. Specific instructions regarding label usage are provided with each shipment. Questions about use of the labels should be directed to Audrey B. McKinnon at (919) 286-0045, ext. 237.

The tracking information provided by the barcode system depends upon the type of form submitted to the DMC. For a form submitted only once per patient (i.e., on-study, background, death), the tracking system indicates if that form has been received and the approximate date of receipt. However, if a form must be submitted more than once (i.e., follow-up, toxicity), the system can only indicate the number of times the form was received and the approximate dates of receipt. The system cannot provide information on the specific reporting periods covered on each form (i.e., "To" and "From" dates on follow-up forms).

### Instructions for using barcode labels

#### PURPOSE:

To enhance the ability of the CALGB Data Management Center to track the receipt of incoming data forms.

#### GENERAL GUIDELINES

- Data management personnel at each main member should forward the barcode labels to the appropriate affiliate institutions upon receipt
- Data management personnel at each institution are responsible for adding the labels to the appropriate CALGB forms before the data are submitted to the DMC.
- Labels are provided for CALGB coordinated studies only.
- Labels should not be used to submit amended or revised data.
- In the event a label is damaged, two reserved additional labels have been provided per form.
- Additional labels should be requested from the appropriate data coordinator before an institution's supply has been depleted.

#### FORM-SPECIFIC INSTRUCTIONS

- Review the information on the label to make sure everything is correct. (Notify the appropriate data coordinator at the CALGB Data Management Center if there are any problems.)
- Continue to complete all header information on the form as a cross-reference.
- Peel off the correct label and place the label in the top left corner of the form. If a multi-page form is being submitted, place one label only on the first page.

## CALGB Web Site Enhancements

Robert Niles, Director of Technical Services

The CALGB Central Office and Statistical Center are in the process of redesigning and enhancing the CALGB Web site. Recent changes include: the addition of protocols in development; access to ECOG-coordinated intergroup protocol documents; an updated roster database and policy and procedures manual; and access to presentations and the CALGB Information Systems Client application.

Several new features are currently in development and will be available by June 1999. These include: access to all CALGB forms for active protocols; real-time access to the roster, including information on participants, committees, and institutions; and a revamped security system allowing more password flexibility.

Demonstrations of the features, functionality, and usability will be held at the 1999 Summer Group Meeting in Toronto.

#### Fast Facts:

**Address (URL):** <http://www-calgb.uchicago.edu>

**Access:** Access to the CALGB members area requires a password. Passwords can only be requested online by filling out a Password Request Form, located at the home page. You must be an active member of the group to receive a password. If you are not an active member, please see the Principal Investigator of your CALGB network for membership information. The CALGB Central Office will need to receive documentation from the Principal Investigator before you can become a CALGB member.

**Technical Requirements:** To use the CALGB Web site you need access to the internet. If you do not currently have access, talk with your system administrator about gaining internet access and a suitable Web browser. For best results, you should use Netscape Navigator 3.0 or Internet Explorer 3.0 or later versions. To download and view certain documents on the CALGB Web site, you will need to use Adobe's Acrobat Reader software. The software is free and instructions for download and installation are located at URL: <http://www-calgb.uchicago.edu/Members/UseInfo.html>. Please consult your system administrator before installing any software on your computer.

#### Web-Site Content:

The site includes information from the following areas:

#### How to use the CALGB Web site.

**CALGB Participant Roster Search:** search the CALGB database by participant name, specialty, institution, or member identification number.

**Meetings:** schedules, travel information, registration forms, and upcoming meeting dates.

**Publications:** online library of *CAL•GAB* and CAPStone newsletters and Group Meeting Minutes Books.

**Administrative:** contact information, Group administrative forms, and the CALGB Policies and Procedures.

#### Committee Membership.

**Protocols:** protocol documents, model consent forms, status sheets, and access to ECOG intergroup protocols.

**Financial:** the latest CALGB Study Funding List and other funding bulletins.

**CALGB IS Client:** download the latest version of the CALGB IS Client.

**Presentations:** download available presentations.

# PROTOCOL NEWS

## NEW STUDIES

### October 15, 1998

**19805**—Phase II study of flavopiridol (NSC#649890) in patients with fludarabine refractory B-cell chronic lymphocytic leukemia.  
*Study Chair: John C. Byrd, M.D.*

### November 15, 1998

**9740**—Cross-sectional study to estimate the incidence of endometrial pathology in women receiving tamoxifen on SWOG S9313 (INT 0137, CALGB 9394, NCCTG 93-50-51). *Study Chair: Larry Norton, M.D.*

**39805**—Phase II trial of 6-hydroxymethylacylfulvene (HMAF; MGI-114) in patients with relapsed or refractory non-small cell lung cancer.  
*Study Chair: Carol A. Sherman, M.D.*

**89804**—Randomized phase III trial of three different regimens of CPT-11 plus 5-fluorouracil and leucovorin compared to 5-fluorouracil and leucovorin in patients with measurable advanced adenocarcinoma of the colon and rectum. *Study Chair: Charles S. Fuchs, M.D.*

### December 15, 1998

**19804**—Phase II study of newly diagnosed patients with BCR/ABL (+) chronic myelogenous leukemia treated with combined homoharringtonine (NSC #141633) and low-dose cytarabine. *Study Chair: Timothy J. Ernst, M.D.*

**29801**—Cytogenetic and molecular monitoring of CML.  
*Study Chair: Wendy Stock, M.D.*

**39802**—Video-assisted lobectomy for peripheral ( $\leq 3$  cm) N0, non-small cell lung cancer: a phase II feasibility study. *Study Chair: Scott J. Swanson, M.D.*

### January 15, 1999

**9872**—Activated protein C resistance and tamoxifen-associated thrombosis.  
*Study Chair: Judy E. Garber, M.D.*

**19802**—Phase II study in adults with untreated acute lymphoblastic leukemia testing increased doses of daunorubicin during induction, and cytarabine during consolidation, followed by high-dose methotrexate and intrathecal methotrexate in place of cranial irradiation. *Study Chair: Wendy Stock, M.D.*

**49805**—Phase III randomized double blind study of letrozole versus placebo in women with primary breast cancer completing five or more years of adjuvant tamoxifen. *Study Chair: Hyman B. Muss, M.D.*

### February 15, 1999

**39804**—Phase III randomized prospective trial of open versus minimally invasive, video-assisted resection of pulmonary metastases.  
*Study Chair: Joshua R. Sonett, M.D.*

## RECENT CLOSURES

### December 1, 1998

**9495**—Induction chemoradiotherapy followed by surgical resection for non-small cell lung cancer involving the superior sulcus (pancoast tumors): a phase II trial. *Study Chair: Frank C. Detterbeck, M.D.*

### December 21, 1998

**9780**—Phase II study of docetaxel, estramustine, and low dose hydrocortisone in men with hormone refractory prostate cancer.  
*Study Chair: Diane M. Savarese, M.D.*

### January 15, 1999

**9170**—Multi-center trial of hospital versus early discharge therapy of low-risk patients with fever and neutropenia: a phase III study (limited access).  
*Study Chair: James A. Talcott, M.D.*

**9235**—Etoposide, cisplatin and radiation therapy with or without tamoxifen in limited stage small cell lung cancer: a randomized phase III study.  
*Study Chair: Edward F. McClay*

**9570**—Development of standard methods for collecting economic data for CALGB trials. *Study Chair: Kevin A. Schulman, M.D.*

**9733**—CPT-11 (Irinotecan) for malignant mesothelioma: a phase II study.  
*Study Chair: Hedy L. Kindler, M.D.*

## CALGB STUDY FUNDING

Support is available to qualifying institutions for participation in these studies. Payments are made through the main member institution. For more information, visit the CALGB website or contact Mary A. Sherrell, Financial Officer at (773) 702-9856.

**9270** – Colorectal Adenoma Prevention Trial Using Aspirin. Phase III Study.

**9334** – Sclerosis of Pleural Effusion by Talc Thoracoscopy vs. Talc Slurry. Phase III Study.

**9335** – Video-assisted Wedge Resection + Radiotherapy for High Risk T1 NSCLC. Phase II Study.

**9380** – Thoracoscopic Staging for Esophageal Cancer. Phase II Study.

**9473** – Omega-3 Fatty Acids for Cancer Cachexia. Phase I/II Trial.

**9481** – Hepatic Artery Floxuridine, Leucovorin, and Dexamethasone vs Systemic 5-FU and Leucovorin as Treatment for Hepatic Metastases from Colorectal Cancer. Phase III Study.

**9484** – Linkage of Molecular and Epidemiological Breast Cancer Investigations with Treatment Data. Specialized Registry.

**9490** – Does an Oral Analgesic Protocol Improve Pain Control for Patients with Cancer? (ECOG E4293)

**9499** – Chemoprevention Trial to Prevent Second Primary Tumors with Low-Dose 13-CIS Retinoic Acid in Head and Neck Cancer. (MDACC DM90-094)

**9581** – Adjuvant Immunotherapy with Monoclonal Antibody 17-1A after Resection for Stage B2 Colon Cancer. Phase III Randomized Study.

**9594** – Intermittent Androgen Deprivation in Patients with Stage D2 Prostate Cancer. Phase III Study. (SWOG 9346)

**9596** – Vincristine, Doxorubicin, and Dexamethasone with or w/o PSC-833 in Patients with Relapsing or Refractory Multiple Myeloma. Phase III Study. (ECOG E1A95)

**9670** – Barriers to Participation of Older Women with Breast Cancer in Clinical Trials. Pilot Study.

**9682** – Prognostic Significance of Endorectal MRI in Predicting Outcome After Combined Radiation and Androgen Suppression for Prostate Cancer. Prospective Phase II Study.

**9730** – Taxol vs. Taxol + carboplatin for advanced NSCLC. Randomized Phase III Study.

**9770** – High-Dose vs Conventional Dose Octreotide Acetate vs Loperamide in the Treatment of Chemotherapy-related Diarrhea in Patients with Colorectal Cancer. Randomized Trial. (ECOG E1295)

**9782** – Phase II trial of potency-sparing hormonal therapy in patients with elevated serum PSA after radiation therapy or radical prostatectomy for prostate cancer.

**9791** – Salvage therapy with paclitaxel and carboplatin vs salvage therapy with stem cell supported carboplatin, mitoxantrone and cyclophosphamide in patients with persistent low volume ovarian cancer.

**9870** – Quality of life and cost analysis of a prospective randomized phase III trial comparing trimodality therapy to surgery alone for esophageal cancer.

**19801** – A Phase II Study of 506U78 in Patients with Refractory or Relapsed T-Lineage Acute Lymphoblastic Leukemia (ALL) or Lymphoblastic Lymphoma (LBL)

# “Thank You” To Organizations and Individuals Supporting CALGB During 1998

The following organizations have generously supported CALGB research, educational programs, publications, and data resources during 1998:

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# CALGB CALENDAR

## Summer '99 Group Meeting

June 25–27, 1999

Toronto, Ontario, Canada—*Sheraton Centre*

REGISTRATION DEADLINE

May 22, 1999

(Meeting Registration and Hotel Reservations)

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## Fall '99 Group Meeting

Nov. 12–14, 1999

Miami Beach, Florida—*Hotel Fontainebleu*

## ABSTRACT DEADLINES

Abstracts reporting on CALGB studies must be submitted to the Central Office for review at least two weeks prior to the submission deadline.

	ABSTRACTS DUE AT CENTRAL OFFICE	SUBMISSION DEADLINE	MEETING DATE	LOCATION
<b>ASH</b> American Society of Hematology	August 16, 1999	Sept. 1, 1999	Dec. 3–7, 1999	New Orleans



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