

CALGB

*Tomorrow's Cancer
Treatments Today*

THE CALGB

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Moving Clinical Cancer Research Forward: A Year in Review for Cancer and Leukemia Group B



Each year, the Cancer and Leukemia Group B invests in clinical cancer research, seeking to improve methods of cancer treatment that will have long-term, beneficial effects for cancer patients and survivors. This year was no different. With a well-balanced research portfolio and superb infrastructure, the CALGB published more than 100 manuscripts and members presented at numerous meetings, reporting on study results that not only have created new cancer knowledge and impacted the lives of cancer patients, but have also contributed to furthering the next generation of clinical trials.

Take for example, the results of CALGB 9710, a study that improved the survival rate of patients with a rare form of cancer (acute promyelocytic leukemia, or APL) by adding arsenic to their standard treatment (see *Leukemia Committee section on page 14*). These results have drawn national attention and have changed the standard of care for APL. Results from a companion study to CALGB 89803, also highly publicized this year, indicated that a high meat and high fat diet (considered "western") may lead to higher rates of recurrence and death among colon cancer survivors (see *GI Committee section on page 14*).

This year, the Group also focused inwardly to improve existing systems and develop

new computing and reporting mechanisms to better serve CALGB members. New features of systems such as the CALGB Reporting System and TeleForm® Web Submit, and enhancements to registration, including the Pre-registration Feature, were released over the summer. Inroads have been made to further develop other systems, including the Routine Adverse Events Reporting System (RAERS) and the Specimen Tracking System, which will replace LabTrak. All remain a priority for the Group.

Highlighting CALGB Research

More than 3,000 oncology specialists from nearly 40 CALGB committees carried out the Group's work this year. Take a closer look at some of the results.

— see **A YEAR IN REVIEW**, page 13

MESSAGE FROM THE GROUP STATISTICIAN



Stephen L. George, Ph.D.

Fast-Tracking Scientific Discovery with Electronic Data Capture System

In the early years of the Cancer and Leukemia Group B (late 1950s), nearly all operations, both scientific and administrative, were performed manually. Fifty years later, technology has allowed us to automate many manual processes, yet the promise of a paperless system has not been realized. Our next step in this direction is the implementation of an electronic data capture (EDC) system for all CALGB studies.

In September 2005, Group Statisticians agreed to move ahead with a joint venture, supported by the Coalition of Cancer Cooperative Groups, to build or buy a common EDC system. All groups agreed to use the new system in order to provide advantages and cost savings for all. While it was initially assumed that building a common system would be the only way to achieve our goals, a subsequent lengthy review of 13 commercial systems led to the decision to adopt one of these available systems.

With input and support from the National Cancer Institute (NCI), this review has produced two finalists and the procurement process has begun. In addition to electronic data collection, these systems provide other advantages. For example, through built-in expectancy systems, each institution will know exactly which forms are expected and in what time frame.

Transition to an EDC system will require significant operational changes for all who currently handle CALGB data. We are not planning simply to automate current processes, thereby transferring inefficiencies in the current system into a new system. But we will use the

EDC system to streamline processes, to provide more immediate feedback on data issues, and to improve the entire data management process. For example, communications between Clinical Research Associates (CRAs) and Data Coordinators (DCs) should be greatly enhanced as the system catches many data errors before they are submitted. Queries will be reduced through automated validation of data.

A common EDC system will also decrease training and IT costs across the groups. The increase in data quality and the improved timeliness of data will help provide more up-to-date data on all studies. An enhancement in timeliness is even more important as more studies are opened across all groups, and through the Cancer Trials Support Unit (CTSUs). Further, as more groups participate in international studies, the benefits of EDC will become even more apparent to study conduct.

As with all joint efforts, the initial setup phase of this project will take time. We will be working with the other cooperative groups to standardize the workflow for data collection. Once this phase is completed, we will begin setting up new studies and testing the software.

As we progressively add new studies to the EDC system, processes and roles will change. The ultimate goal is to move scientific discovery along at a faster pace. In the next year, you will receive more information regularly as we move toward implementing the new system.

CALGB Develops Global Study Across Three Continents to Treat Acute Myeloid Leukemia Patients



10603 A phase III randomized, double-blind study of induction (daunorubicin/cytarabine) and consolidation (high-dose cytarabine) chemotherapy + midostaurin (PKC412) (IND #TBD) or placebo in newly diagnosed patients < 60 years of age with FLT3 mutated acute myeloid leukemia (AML)

The Cancer and Leukemia Group B plans to launch a study to treat acute myeloid leukemia patients that spans three continents and eight countries, including leukemia centers in the United States, Canada, Germany, Italy, Spain, Brazil, Belgium, and the Netherlands. Chaired by Richard Stone, M.D., of Dana-Farber Cancer Institute, CALGB 10603—A phase III randomized, double-blind study of induction (daunorubicin/cytarabine) and consolidation (high-dose cytarabine) chemotherapy + midostaurin (PKC412) (IND# TBD) or placebo in newly diagnosed patients < 60 years of age with FLT3 mutated acute myeloid leukemia (AML)—will compare in 500 patients the effects of a standard chemotherapy regimen for AML that includes the drugs daunorubicin and cytarabine combined with or without midostaurin (also known as PKC412), to determine which is better. Patients will receive either the investigational agent, midostaurin, combined with daunorubicin and cytarabine or placebo combined with daunorubicin and cytarabine.

Midostaurin, a multi-targeted kinase inhibitor, has been tested in more than 400 patients and is being studied in a number of illnesses, including AML, colon cancer and lung cancer. Midostaurin blocks an enzyme, produced by a gene known as FLT3, that may have a role in the survival and growth of AML cells. Midostaurin has not been approved by the Food and Drug Administration (FDA).

The study will select patients based on the presence of a FLT3 mutation. Use of a targeted agent against a targeted population is thought most likely to offer the greatest improvement in efficacy. The greater activity of the drug

in FLT3^{mut} patients is predictive of greater clinical benefit. Furthermore, a trial conducted exclusively in FLT3^{mut} patients could demonstrate the highest likelihood of a positive result while requiring the smallest number of patients when compared to a trial design that includes both FLT^{WT} and FLT3^{mut} patients (i.e., an enrichment strategy for a target agent).

CALGB 10603 is being endorsed by the Eastern Cooperative Oncology Group (ECOG), Southwest Oncology Group (SWOG) and the National Cancer Institute of Canada Clinical Trials Group (NCIC CTG). The following groups will participate in the study: Gruppo Italiano Malattie e Matologiche dell'Adulto (GIMEMA ONLUS Foundation) in Italy; European Organization for Research and Treatment of Cancer (EORTC) in the Netherlands; German Austrian Acute Myeloid Leukemia Study Group (German-Austrian AMLSG) in Germany; Study Alliance Leukemia (SAL) in Germany; Programa Español para el Tratamiento de las Hemopatías Malignas (PETHEMA) in Spain; and Grupo Cooperativo de Tratamiento de las Leucemias Agudas y Mielodisplasias (CETLAM) in Spain.

CALGB Breast Cancer Study to Combine Antiangiogenesis Agent with Standard Endocrine Therapy



40503 Endocrine therapy in combination with anti-VEGF therapy: a randomized, double-blind, placebo-controlled phase III trial of endocrine therapy alone or endocrine therapy plus bevacizumab (NSC #704865; IND #7921) for women with hormone receptor-positive advanced breast cancer

According to the American Cancer Society, more than 40,000 women are expected to die from breast cancer this year. Research shows that antiangiogenesis therapy can delay disease progression when added to chemotherapy, representing a significant advancement in the care of women with breast cancer. CALGB 40503—Endocrine therapy in combination with anti-VEGF therapy: a randomized, double-blind, placebo-controlled

— see **SPOTLIGHT ON CALGB TRIALS**, next page

The **CAL·GAB** is published by the Cancer and Leukemia Group B quarterly and distributed to CALGB active membership through the CALGB Web site (www.calgb.org). Suggestions for articles are encouraged. Contributions for the Spring 2008 issue are due January 22, 2008. Forward articles, suggestions and other correspondence to jowens@uchicago.edu.

The **CAL·GAB** reserves the right to make corrections, changes and deletions in submitted copy in conformity with the newsletter's editorial policies.

SPOTLIGHT ON CALGB TRIALS / 40503 and 30607

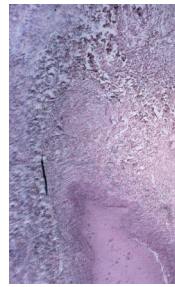
continued from page 3

phase III trial of endocrine therapy alone or endocrine therapy plus bevacizumab (NSC #704865; IND #7921) for women with hormone receptor-positive advanced breast cancer—will determine whether the addition of bevacizumab to standard endocrine therapy can improve the effectiveness of therapy compared to endocrine therapy alone in 360 women. It will evaluate whether anti-VEGF (vascular endothelial growth factor) therapy with bevacizumab can delay the development of resistance and prolong progression-free survival when added to first-line endocrine therapy for hormone-receptor positive metastatic breast cancer.

Standard endocrine therapy for breast cancer includes drugs such as tamoxifen or aromatase inhibitors. Bevacizumab, an anti-angiogenic agent, targets the tumor vasculature, and has been shown to be effective when added to chemotherapy for patients with metastatic disease. Laboratory studies suggest that anti-VEGF therapies such as bevacizumab may make standard endocrine treatments such as tamoxifen and aromatase inhibitors more effective in controlling breast cancer. This study also includes four correlative science studies based on tissue, blood, biomarkers and pharmacogenomics.

The Study Chair is Maura Dickler, M.D., of Memorial Sloan-Kettering Cancer Center. CALGB 40503 is being endorsed by Eastern Cooperative Oncology Group (ECOG). This study is currently in development.

Targeted Therapy Main Focus of New CALGB Lung Cancer Trial



30607 Randomized, phase III, double-blind placebo-controlled trial of sunitinib (NSC #736511, IND #74019) as maintenance therapy in non-progressing patients following an initial four cycles of platinum-based combination chemotherapy in advanced, stage IIIB/IV non-small cell lung cancer

Taking a closer look at targeted therapy and figuring out how best to use it is the focus of a new CALGB lung cancer trial in development. CALGB Study Chair Mark Socinski, M.D., of the Lineberger Comprehensive Cancer Center at the University of North Carolina at Chapel Hill, will study targeted therapy as maintenance treatment in lung cancer patients in CALGB 30607—Randomized, phase III, double-blind placebo-controlled trial of sunitinib (NSC#736511, IND #74019) as maintenance therapy in non-progressing patients following an initial four cycles of platinum-based combination chemotherapy in advanced, stage IIIB/IV non-small cell lung cancer.

With 156 participants, this study will determine whether administering the drug sunitinib after a patient responds to chemotherapy (i.e., the tumor shrinks or stops growing) will help the tumor continue to shrink, or stay the same. Sunitinib, a tyrosine kinase inhibitor approved by the Food and Drug Administration in 2006 for the treatment of renal cell carcinoma and imatinib-resistant gastrointestinal stromal tumors (GIST)¹, is an investigational agent in the treatment of non-small cell lung cancer. Standard treatment for advanced, stage IIIB/IV non-small cell lung cancer would be to stop chemotherapy treatment after the patient receives initial therapy.

A correlative science and quality of life study will be included in CALGB 30607. The effects of sunitinib will be examined in the quality of life study and will focus on physical symptoms and functioning, mood and the patient's social life. This study will also provide insight on how patients feel during treatments, along with the effects of treatment.

The correlative science study, an initial pharmacogenetic investigation, will determine how to better personalize antiangiogenic therapy. The investigators will determine the relationship between patients' genes in the vascular endothelial growth factor (VEGF) signaling pathway and the concentration of plasma proteins that affect angiogenesis. This study should help determine which patients are more likely to benefit from drugs like sunitinib.

Source

1. Faivre S, Delbaldo C, Vera K, Robert C, Lozahic S, Lassau N, Bello C, Deprimo S, Brega N, Massimini G, Armand J P, Scigalla P, and Raymond E. Safety, pharmacokinetic, and antitumor activity of SU11248, a novel oral multitarget tyrosine kinase inhibitor, in patients with cancer. *J Clin Oncol*, 24: 25-35, 2006.



The Cancer and Leukemia Group B presented nine abstracts at the American Society of Hematology (ASH) 49th Annual Meeting and Exposition December 8-11, 2007 in Atlanta, GA. The abstracts are listed here with a spotlight on two: CALGB 19808 and CEBPA mutations in CN AML.

Phase III trial of immunotherapy with recombinant interleukin-2 (rIL-2) versus observation in patients < 60 years with acute myeloid leukemia (AML) in first remission (CR1): Preliminary results from Cancer and Leukemia Group B (CALGB) 19808

Kolitz JE, Hars V, DeAngelo DJ, Allen SL, Shea TC, Vij R, Hoke E, Bloomfield CD, Caligiuri MA, George SL, Larson RA

The CALGB evaluated the use of rIL-2 for immunotherapy of minimal residual disease in a phase III trial in patients with AML in first CR after completing all planned chemotherapy. The rationale supporting the use of rIL-2 in this setting includes its ability to effect antigen-independent cytotoxicity against AML blasts, its non-cross resistance with cytotoxic agents, and its ability to expand cytotoxic T and natural killer (NK) cells. Pts < 60 years with untreated non-M3 AML were eligible. 734 patients were enrolled. The first 302 patients were randomized between 2 induction regimens: Ara-C, Daunorubicin, and Etoposide (ADE) or ADEP with the P-glycoprotein modulator PSC-833 (Kolitz et al, ASH 2005). The remaining 432 patients received ADE induction. Post-remission therapy was based on cytogenetic risk factors: patients with Core Binding Factor (CBF) AML received 3 courses of High-Dose Ara-C (HiDAC), while all others were assigned to receive a 2 step autologous transplant (ASCT) regimen (Linker et al, *Biol Blood Marrow Transpl* 2000). Randomization between rIL-2 and observation was to occur no later than 120 days after day 1 of the last HiDAC cycle or day 0 of ASCT, as soon as the neutrophil count > 750/ μ L, platelets > 50,000/ μ L with bone marrow showing a leukemia-free state and trilineage maturation and recovery from non-hematological toxicity to < grade 2. The 90 day immunotherapy regimen consisted of low-dose rIL-2 sequences for expanding cytotoxic effector cells and brief, higher dose bolus treatments aimed at activating them. rIL-2 was given SC at 1×10^6 IU/m² on days 1-14, 19-28, 33-42, 47-56, 61-70 and 75-90, and $12-15 \times 10^6$ IU/m² on days 15-17, 29-31, 43-45, 57-59 and 71-73. CR was achieved in 77% of evaluable patients. After HiDAC consolidation or ASCT, patient refusal, early relapse, and delayed blood count recovery accounted for nearly all failures to undergo randomization to IL-2 or observation. The distribution of patients with CBF and non-CBF AML was comparable between the randomized arms. The median follow-up time from the post-remission randomization date for the surviving patients

is 29 months. By intention-to-treat, for the 214 randomized patients, the 3-year disease-free survival rate is 45% (95% CI: 35%,56%) on the observation arm and 56% (47%,67%) on the rIL-2 arm ($p=0.11$; logrank test); the 3-year overall survival rate is 61% (52%,72%) for patients randomized to observation and 68% (58%,79%) for the rIL-2 arm ($p=0.09$). Twenty-nine of the 107 patients randomized to rIL-2 therapy either refused to receive rIL-2 or were unable to start because of unresolved toxicities; another 28 patients started treatment but failed to complete their 90-day course. Grade 4 toxicities were neutropenia (17%), thrombocytopenia (11%), febrile neutropenia (FN, 1%), increased bilirubin (1%) and hypocalcemia (1%). Grade 3 toxicities, observed in 10%-14% of patients, were hypotension, fatigue, dehydration and FN. We conclude that post-consolidation immunotherapy with 90 days of rIL-2 is tolerable but not well accepted by patients and/or physicians. Further follow-up and additional analyses are planned, correlating outcomes with clinical subsets, amount of rIL-2 therapy received, as well as measurements of ex vivo cytotoxicity mediated by patients effector cells against cryopreserved autologous AML blasts. [Abstract #57]

Gene and microRNA (miRNA) expression signatures and prognostic significance of CEBPA mutations in cytogenetically normal (CN) acute myeloid leukemia (AML) with high-risk molecular features: A Cancer and Leukemia Group B (CALGB) study.

Marcucci G, Maharry K, Radmacher MD, Mrózek K, Vukosavljevic T, Paschka P, Whitman SP, Langer C, Baldus CD, Ruppert AS, Powell BL, Carroll AJ, Caligiuri MA, Kolitz JE, Larson RA, Bloomfield CD

Although CEBPA mutations have been reported to predict favorable outcome in CN-AML, their prognostic value has not been simultaneously evaluated in the context of such established prognostic molecular markers in CN-AML as the combination of FLT3-ITD and NPM1 mutational status and BAALC and ERG expression. 169 adult patients (pts) aged <60 years (yrs) with untreated, de novo CN-AML, enrolled on CALGB protocols 9621 or 19808 that include autologous stem cell transplantation for consolidation, were analyzed for CEBPA mutations by DNA PCR amplification and direct sequencing. Testing for BAALC and ERG expression, FLT3-ITD, FLT3-TKD, MLL-PTD and NPM1 mutations (NPM1+) was performed centrally in pretreatment marrow or blood samples. Unexpectedly, pts with CEBPA mutations (CEBPA+) were more likely to have FLT3-ITD/NPM1 high-risk molecular features [i.e., FLT3-ITD+ and/or NPM1 wild-type (NPM1-)] than low-risk molecular features (FLT3-ITD-/NPM1+; 26 v 3 pts, respectively; $P=.001$). Thus, we focused subsequent analyses on FLT3-ITD/NPM1 high-risk molecular feature

CALGB 2007 ASH ABSTRACTS

pts (n=109) that included 90% of the CEBPA+ cases. In this group, a microarray gene-expression signature of 2,342 probes, 59% of which were downregulated in CEBPA+ pts, separated CEBPA+ and CEBPA wild-type (CEBPA-) pts [false discovery rate (FDR) for the signature=.01]. Among the 20 most downregulated probes in CEBPA+ pts, 9 corresponded to a variety of Homeobox genes (HOXA3, A5, A9, A10, B2, B3, MEIS1). Also downregulated in CEBPA+ pts were other Homeobox genes (HOXA1, A2, A4, A6, A7, B4, B5, B6), FLT3, RUNX1 and RAS superfamily members, while CEBPA and GATA1 were upregulated. Additionally, a 13-probe microRNA (miRNA) expression signature distinguished CEBPA+ from CEBPA- pts (FDR=.11). This signature shared common features with a previously reported miRNA-signature predictive of clinical outcome in FLT3-ITD/NPM1 high-risk molecular feature CN-AML (Radmacher et al. JCO 2007;25:359s). Eight miRNA probes for mature members of the miRNA 181 family were upregulated in CEBPA+ pts; an association between miRNA 181 family upregulation and good outcome was a major feature of the previously reported outcome miRNA signature. Additionally, a probe for miRNA 194, whose downregulation was associated with good outcome in the prior outcome signature, was also downregulated in CEBPA+ pts. Consistent with these findings, we observed that CEBPA+ status was indeed predictive of better outcome in the FLT3-ITD/NPM1 high-risk molecular feature group. CEBPA+ pts had a better EFS than CEBPA- pts (P<.0001), with estimated 3-yr EFS rates of 57% and 17%, respectively. In a multivariable analysis, CEBPA mutations independently predicted longer EFS (P=.0004; hazard ratio=0.30; 95%CI=0.15-0.58), after adjusting for ERG expression (P=.03). In summary, we report that among CN-AML, CEBPA+ pts mostly have FLT3/NPM1 high-risk molecular features, and that based on the presence or absence of CEBPA mutations this high-risk molecular features group can be subdivided into 2 subsets characterized biologically by strong gene- and miRNA-expression signatures and clinically by different outcomes. It is likely that testing for CEBPA mutations at diagnosis will improve molecular risk-based classification of de novo CN-AML and aid in risk-adapted treatment stratification. Gene- and miRNA-expression profiling may provide insights into disease biology that result in development of novel therapies. [Abstract #104]

>> Leukemia Committee

CALGB 9011, 9712, 19901

Alemtuzumab increases serious infections in patients with previously untreated chronic lymphocytic leukemia (CLL) receiving fludarabine-based therapy: A comparative analysis of 3 Cancer and Leukemia Group B studies (CALGB 9011, 9712, 19901).
Morrison VA, Peterson BL, Rai KR, Byrd JC, Larson RA

for the Cancer and Leukemia Group B, Chicago, IL. [Abstract #756]

CALGB 9720

Cytarabine, daunorubicin and etoposide (ADE) chemotherapy in acute myeloid leukemia (AML) patients ≥60 Years (CALGB 9720).

Baer MR, George SL, Sanford BL, Bothun SM, Mrózek K, O'Loughlin KL, Kolitz JE, Moore JO, Stone RM, Powell BL, Caligiuri MA, Bloomfield CD, Larson RA for the Cancer and Leukemia Group B, Chicago, IL. [Abstract #296]

CALGB 10001

Autologous stem cell transplantation (SCT) following sequential chemotherapy and imatinib for adults with newly diagnosed Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL) – CALGB 10001.

Wetzler M, Stock W, Donohue KA, Owzar K, Sher DA, Hoke EE, McCarty JM, Blum WG, Powell BL, Bloomfield CD, Linker CA, Larson RA for the Cancer and Leukemia Group B, Chicago, IL. [Abstract #2869]

CALGB 10102

Quantitative measurement of CD52 expression and alemtuzumab binding in adult acute lymphoblastic leukemia (ALL): Correlation with immunophenotype and cytogenetics in patients (pts) enrolled on a phase I/II trial from the Cancer and Leukemia Group B (CALGB 10102).

Lozanski G, Sanford B, Mrozek K, Edwards C, Pearson R, Bloomfield CD, Larson RA, Stock W (Intr. by Stock W) for the Cancer and Leukemia Group B, Chicago, IL. [Abstract #2386]

>> Leukemia Correlative Sciences Committee

CALGB 8461, 9665, 20502

Wilms tumor 1 (WT1) gene mutations predict poor outcome in adults with cytogenetically normal (CN) acute myeloid leukemia (AML): A Cancer and Leukemia Group B (CALGB) study.

Paschka P, Marcucci G, Ruppert AS, Mrózek K, Whitman SP, Maharry K, Langer C, Baldus CD, Powell BL, RPCI, Carroll AJ, Caligiuri MA, Kolitz JE, Larson RA, Bloomfield CD for the Cancer and Leukemia Group B, Chicago, IL. [Abstract #362]

>> Lymphoma Committee

CALGB 50203

Doxorubicin, vinblastine and gemcitabine (AVG), a novel regimen excluding bleomycin for the treatment of early stage hodgkin lymphoma (HL): Results of CALGB 50203.

Straus D, LaCasce A, Bartlett N, Juweid M, Kostakoglu L, Hall N, Johnson J, Jung SH, Canellios G, Schwartz L, Cheson B for the Cancer and Leukemia Group B, Chicago, IL. [Abstract #214]

Imaging Correlative Studies and the Role of the CRA

By *Howie Weiner, C.C.R.P., University of Chicago, Section of Hematology/Oncology*

The last two issues of the *CAL-GAB* newsletter featured important articles on the new Imaging Core Laboratory and separately, the role of the Clinical Research Associate (CRA) in correlative science protocols. This commentary combines the two in further exploring the critical role of the CRA in procuring accurate and timely imaging data that will support the development of imaging correlative science as a vital component of clinical trials.

Taking an Active Approach

A close examination of one protocol where an imaging correlative study plays an important role can highlight the active approach the CRA needs to adopt in executing the intent of the study. CALGB 80302 (A phase II trial of preoperative irinotecan, cisplatin and radiation in esophageal cancer) contains a PET (positron emission tomography) imaging sub-study (CALGB 580601) that presents an array of challenges to the CRA in its implementation. The study calls for the acquisition of PET imaging digitally at three time points:

- Baseline (prior to study treatment).
- Day 15-19 post initiation of induction chemotherapy (during induction chemo). A research-mandated PET reimbursed by the study.
- Within seven days *prior* to Day 1 of concurrent chemoradiotherapy.

Simply, the goal of the correlative study will be to determine whether changes in the intensity of the PET uptake measured in standardized uptake value (SUV) are “predictive of response at surgery and survival. PET scan assessment of response during induction chemotherapy may provide a strategy to assess response early on during adjuvant therapy, and direct a change in therapy if a response is not observed.”

The role of the CRA seems straightforward enough – to simply acquire the required scans at protocol-specified time points, and submit them to the CALGB Imaging Core Laboratory (ICL). But a closer examination reveals some challenging issues. One important issue is that PET scans need to be done according to protocol specifications, which may vary from an institution’s standard procedure.

For example, the protocol states, “Sixty minutes after the administration of FDG, two or three dimensional whole body emission scans...will be obtained.” However, some institutions utilize a 90-minute time period between injection and scanning. If scanning is not done according



to protocol guidelines, it becomes difficult to accurately assess PET response. The protocol states, “It must be ensured that the images at all sites are reconstructed according to the algorithms described...and with the same spatial resolutions.” In other words, replication of the same PET imaging techniques at different institutions is paramount to the study’s success.

Another area of concern is completing the C-1720 80302 FDG-PET Adjunctive Data Form. A clinical description of the PET Imaging process is what is mostly required. Items such as the “Pre-injection FDG syringe dose,” “Emission Scanning Start and Finish Time,” and “Is any radiotracer infiltration at injection site noted,” are neither found in radiology reports or readily available to the CRA. The form can only be completed with the assistance of the Nuclear Medicine Staff.

Becoming the “Point Person”

Thus, the CRA needs to develop an effective strategy to implement the embedded companion study. Most knowledgeable about the details of the protocol and, in effect, charged with its successful execution, the CRA becomes the “point person” in assembling the team approach necessary to carry out the work. The following are some suggestions that may prove helpful.

ONCOLOGY NURSING PERSPECTIVE

MISSION: EDUCATION



By Kathy Klinger, M.S.N., N.P.-C., A.O.C.N., Hematology-Oncology Associates of Central New York

The Cancer and Leukemia Group B Oncology Nursing Committee (ONC) meets at each CALGB Group Meeting, and also twice annually at the CALGB Committee meetings. This year, the ONC added a number of phone conferences to discuss defining the mission and vision for our future in the CALGB. While we have many avenues of involvement, including nursing research, protocol review from the nursing perspective, and participating as liaisons to other CALGB committees, one consistent theme is providing education to nurses, allied health professionals, patients, and the public.

Gail Donnery, M.S.N., A.N.P., O.C.N., of State University of New York Upstate Medical University, heads the Education Subcommittee and coordinates educational sessions at each Group Meeting. Some of these have been joint educational sessions with other groups, some focused primarily on nursing.

But the bottom line is – if you cannot attend a CALGB Group Meeting, you cannot benefit from the education session. Many state licensing requirements, and most credentialing organizations require continuing education. We gave some thought to providing CAL-GAB newsletter articles with continuing education units (CEUs), but that is limited also. So why reinvent the wheel? There are numerous Web-based educational programs that can be done anytime. I am sure many of you have used Web-based programs, but for those who have not, here is a brief overview of some Web sites to visit.

www.nurseceu.com

This Web site offers a practice-focused directory including oncology, NP, geriatric, hospice, and state mandated courses. Nurseceu.com does not directly offer courses, but compares online classes from a variety of CE providers. One category is “Free CEUs for Nurses.” Other courses range from \$10 to \$100 (most in the \$10 to \$40 range). Accreditation varies depending on the provider.

www.worldwidelearn.com

This general education site links to degree programs and continuing education courses. When choosing continuing education, the site links directly to www.CEU4U.com. Select your discipline from a list of available courses. Under nursing, there is a long list categorized by specialty. The oncology section has a notation “Meets Onc-Pro Criteria.” The courses run roughly \$15 per 1 CEU. There is a discount for buying larger numbers of CEU hours and applying them to a variety of courses. This site also has some state-mandated courses.

www.medi-smart.com/freeceu.htm

This is another site that does not directly provide courses, but links to sites that do. It directs you to numerous free courses provided by the American Nurses Association, MediCom, Medscape Nurses CE Center, Meniscus, Power Park, Sigma Theta Tau and the American Red Cross.

www.allnurses.com

While not a direct provider, this site defines itself as a “nursing community.” The continuing education section gives a brief description of sites with a rating (including the number of votes that comprised the rating). Currently, the number of links are limited. The site does, however, have a nice discussion forum listed by state or level of practice (i.e., L.P.N., R.N., N.P.).

www.rn.com

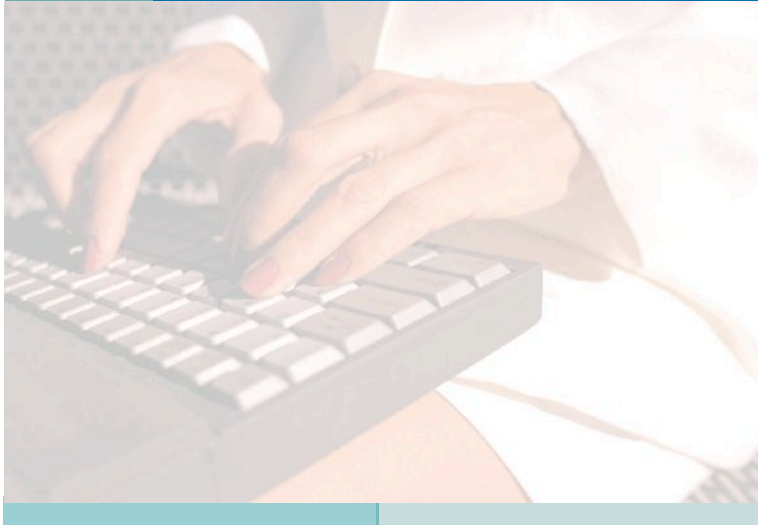
This site lists about 175 ANCC-accredited courses and 400 contact hours. The courses are also accredited by the Oncology Nurses Association. Courses typically run \$5 to \$20, but you can join the “Unlimited Education Club” for \$31.95 annually and take as many courses as you desire. You can try it out using “This month’s free course,” the free course changes periodically. The large section “RN Assessment Series,” which costs \$5-\$10 each course, covers assessment by body region or system. Although there is no oncology section, there are oncology courses included in acute care and other areas.

www.nursingsociety.org

This is the Sigma Theta Tau International Honor Society of Nursing site. Courses are categorized by clinical interest area, and cost \$12. They are discounted if you register on the site. Like some other providers, you can choose to pay \$45.95 (non-members) or \$35.95 (members) for unlimited access to CEUs. There is an oncology course section. Sigma Theta Tau is accredited through the ANCC. This site also offers modular courses including a nurse manager certificate program.

— see **ONCOLOGY NURSING**, next page

ONCOLOGY NURSING PERSPECTIVE



Some Other Sites to Consider:

www.nursingceu.com – Can print courses, pay at the time of test by mail or online.

www.corexcel.com/online.courses.desc.htm - Can repeat online test up to three times.

www.learnwell.org – Includes some wellness courses, healing meditation; less clinical.

www.medscape.com – Can print modules; mostly CME, some CEU credit courses.

The selection presented here is certainly not exhaustive. It is important to note that the CALGB does not specifically endorse any of these sites, so you must look carefully at accreditation of the providers.

Our goal is to foster an atmosphere of lifelong learning to keep nursing practice updated and relevant. We would enjoy seeing a huge nursing contingent at each CALGB Group Meeting. But if you cannot be there, keep up-to-date with local and online education.

In the words of Carl Rogers, a noted psychologist: *“If we value independence, if we are disturbed by the growing conformity of knowledge, of values, of attitudes, which our present system induces, then we may wish to set up conditions of learning which make for uniqueness, for self-direction, and for self-initiated learning.”*

continued from page 7

www.netce.com

Courses found on this Web site are sorted by profession, jurisdiction (state) or by education category. There are some free courses, and some special offers that bundle courses together at one price. Most courses run \$10 to \$39. Course list includes accrediting organization, and the courses can be printed in PDF format to read. Site allows you to build a profile, track courses completed, print certificates, and track courses in progress.

CRA PERSPECTIVE

continued from page 7

- Develop a team early in the process before the first patient is put on protocol. This means distributing the protocol to the relevant Department of Nuclear Medicine staff, including radiologists and technicians, involved in PET imaging. Guarantee that the protocol imaging criteria are understood prior to the opening of the study.
- Be a conduit. Communication is essential and the CRA needs to be the link between medical oncologists, radiologists, clinic coordinators, nuclear medicine technicians, and personnel who will provide digital copies of PET scans. Problems inevitably arise and effective lines of communication can ameliorate any unexpected snags.
- Provide a schedule of the patient's scans to all involved staff and specifically indicate that these imaging studies are part of a research clinical trial.
- Establish contact with the CALGB Imaging Core Laboratory. The lab, which can be easily accessed at www.calgb@imagingcorelab.com, has resources and the expertise to address particular questions that may occur. The lab serves as a real-time resource in performing the work.

Leading Imaging Technologies

The CALGB Imaging Core Laboratory provides our group with a leading edge in developing imaging technologies as an important predictive tool that can greatly enhance the effectiveness of clinical research. Several other CALGB protocols, including CALGB 140503 and CALGB 50303, also contain embedded imaging studies and even more requirements for compliance. This article is meant to be the beginning of a discussion of the strategies needed to carry out these studies. This work is in development, and the CRA, working in an organized, efficient manner, can play a key role in bringing the enormous potential of this field to fruition.

QUALITY ASSURANCE

The Ones That Got Away: New CALGB Policy for Patients Lost to Follow-up

*A researcher whose name we'll not say
Reported his data this way:*

One-third are alive,

One-third of them died,

And the last darn case got away.

—Paraphrased from George Shambaugh, Jr.
former editor-in-chief, *Annals of Otolaryngology*

Clinical Research Associates and Oncology Nurses value the contributions their patients make to the outcome of cancer clinical trials research. By submitting timely and complete protocol-required data, they honor their patients' commitment to finding new cancer therapies. But sometimes, despite the tenacity of the research team, patients "get away" and cannot be found: they move; they choose to be followed elsewhere; sometimes they die.

The CALGB recognizes the importance of complete follow-up in the analysis of a study. Lost patients can lead to incomplete study outcome data and compromise the achievement of study goals (*see Quality Assurance, page 17*). By requiring that lost patients continue to appear in delinquency lists and in delinquency calculations, the Group underscores the value of pursuing lost patients to capture missing data. However, the CALGB Board of Directors recently acknowledged that some patients are conclusively lost and it is an inappropriate use of data management resources to continue to pursue them. In June 2007, the Board approved a policy that provides institutions with a procedure for removing such lost patients from delinquency lists and calculations. This policy will become effective December 15, 2007 and will be phased in during a six-month transition period.

New Procedure for Patients Lost for More than Two Years

Under the new policy, after an institution has tried unsuccessfully for two years to contact a patient, the institution may provide the CALGB Statistical Center with the new CALGB Confirmation of Lost to Follow-up form, which asks for limited details about the follow-up procedures that were used by the institution. The institution must indicate on the form that:

- No date of death can be found in the Social Security Death Index, *and*
- A certified or registered international letter has been



returned unclaimed or marked addressee unknown, or it has been received (as documented by return receipt) but has resulted in no response from the patient over a one-month period after it was received.

The Statistical Center does not require submission of additional details of the attempts to contact the patient, but documentation of the attempts must be retained in the patient's institutional research record for use in audits. Once the Statistical Center receives and approves the Confirmation of Lost to Follow-up form, the patient is no longer considered delinquent.

Continuing Responsibilities for Data Submission

If a patient is confirmed lost, the institution continues to be responsible for submitting protocol-required data (e.g., on-study, treatment, follow-up information) for the period from patient registration through the date of last contact with the patient. Missing data from this period may be considered delinquent in institutional performance evaluations and in audits. These data may be requested in queries from the Statistical Center.

If a patient who is confirmed lost is later found, data submission requirements will depend upon the patient's survival and disease statuses. More information about data submission requirements and other details of the new procedures can be found in the CALGB Policies and Procedures Manual (Chapter 8) on www.calgb.org.

A Threshold for Lost Patients to be Established

The Board of Directors requested the establishment of an acceptable level of lost patients per network. This threshold will be determined by the end of 2008 and will be communicated to the Group.

— see **QUALITY ASSURANCE**, page 17

Reference

Woolard RH, M.D., Carty K, LIC.S.W., Wirtz P, Ph.D., Longabaugh R, Ed.D., Nirenberg TD, Ph.D., Minugh PA, Ph.D., Becker B, M.D., M.P.H. and Clifford PR, Ph.D. "Research Fundamentals: Follow-up of Subjects in Clinical Trials: Addressing Subject Attrition." *Acad Emerg Med* Volume 11, Issue 8 859-866.

Quick Tips for TeleForm® Web Submit and Enhanced CALGB Reporting System

TeleForm® Web Submit

Here are some tips for using TeleForm Web Submit, a forms format that allows CRAs to submit certain study data forms electronically.

- Use the Microsoft® Internet Explorer browser.
- Use the Adobe® Reader® or Adobe Acrobat® Standard or Professional to process and submit the forms. CALGB IS recommends using Version 8 or higher.
- To save the form to your computer and complete and submit it later, use Adobe Acrobat Standard or Professional. Adobe Reader cannot be used.
- If you make a mistake and cannot change an item you have entered, click the **Reset** button and all of your entries will be cleared.
- For decimal fields, either leave all boxes blank if the value was not collected, or include zeros as needed to fill all the boxes. Once you press **Tab** or **Enter**, the numbers will align properly.

<p>Don't type this:</p> <div style="border: 1px solid black; padding: 5px; margin: 5px;"> <p style="text-align: center;">Longest diameter of lesion(s)</p> <hr/> <p>1.5] cm</p> </div>	<p>Do type this:</p> <div style="border: 1px solid black; padding: 5px; margin: 5px;"> <p style="text-align: center;">Longest diameter of lesion(s)</p> <hr/> <p>01.50] cm</p> </div>
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- For decimal fields, be sure to type the decimal even though it is shown on the form. Omitting the decimal is the most common mistake, and will result in the data being submitted without the decimal.

<p>Don't type this:</p> <div style="border: 1px solid black; padding: 5px; margin: 5px;"> <p style="text-align: center;">Longest diameter of lesion(s)</p> <hr/> <p>0123] cm</p> </div>	<p>Do type this:</p> <div style="border: 1px solid black; padding: 5px; margin: 5px;"> <p style="text-align: center;">Longest diameter of lesion(s)</p> <hr/> <p>01.23] cm</p> </div>
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- If you have problems with a form, call the CALGB Help Desk at (877) 442-2542 and provide the form number, version, and field that is causing the problem. The CALGB Help Desk can report the difficulty to the form's designer and the problem will be corrected.
- Updated forms are released on the 15th of each month.

For additional information refer to the Job Aid "Electronic Submission of CALGB Data Forms" located in the Open Access Training section under the Training tab on the CALGB Member Site at www.calgb.org.

CALGB Reporting System

The CALGB Reporting System has been updated by CALGB IS with the additional features CALGB members requested.

- Previously you could organize your list of available reports by category or by report name. Now you can also organize the list to show only reports you have run recently.
- For each report, you can add a label that appears next to the report name in lists.
- You can search reports by comment or by label.
- You can delete reports you have run.

Here's an example of how you might use these features. Imagine that you run four or five reports often, but you have 50 reports available to you. Imagine that you run one report—the Institution Patient Listing—every Friday during the month, and finish with a month-end report.

When **Recently Run** is the selected report organization, you can choose to run the report from a short list of reports rather than the longer lists that would appear if the **Categories** or **Alphabetical** organizations were selected.

calgb.org > Member Site > Reporting System

Reporting System

The CALGB Reporting System allows participants to run, schedule, and view a variety of CALGB-related reports.

Reports

Categories Alphabetical Recently Run

- Reports (Recently Run)
 - Institution Patient Listing
 - Study Status
 - Study IRB Status
 - CALGB Studies in Development

When you're ready to run the Institution Patient Listing, you can add a label, for example Nov 2007

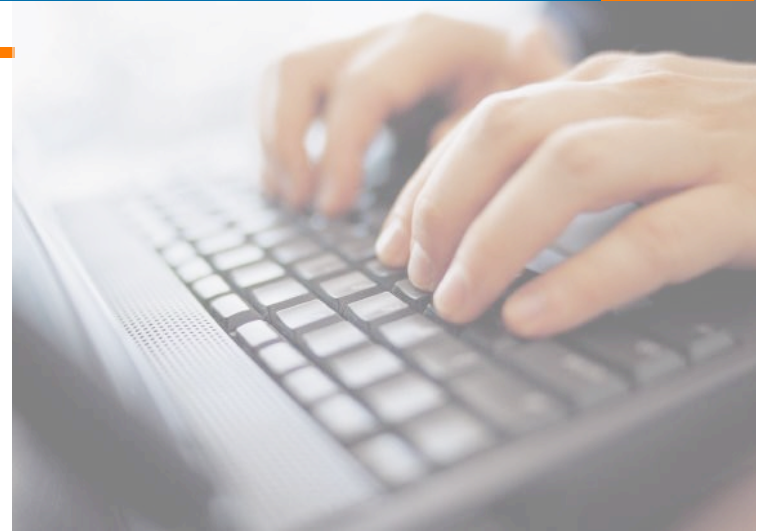
TRAINING UPDATE

CALGB Introduces More Online Training Courses

With the March launch of the new CALGB Training Section on www.calgb.org, CALGB members now have more options to participate in Web conferences and online training. New modules are planned and will come online soon.

For example, the CALGB HIPAA Training Module, which will focus on issues specific to CALGB that are not covered in standard institutional HIPAA training, will be available soon. This online module will clarify the application and definition of Protected Health Information (PHI) and how to send it. It will be offered in two ways: online and as a printed offline version for those without computer access. The online version will be tracked in the CALGB Online Training System (Adobe Connect).

The module will contain interactive elements such as text and image rollovers, hyperlinks to documents and Web pages, and branching capabilities. Branching is designed to deliver specific security information to CALGB Statistical Center employees, including tutorials on how to set Lotus Notes



security features. Branching will also provide an option to review a Secure Mail tutorial. A 10-question assessment based on the course's objectives will end the module.

In addition, a training module presented during CRA Orientation will also be available soon. The Statistical Center Institutional Performance Evaluation Tools Training Module will provide an overview of tools the Institutional Performance Evaluation Committee (IPEC) uses to evaluate institutional performance. This module will be accessible online for CALGB members to take any time.

More information about these and other online modules will follow in future columns.

IS CORNER continued from page 11

Week 1. Subsequent runs could be Nov 2007 Week 2, Nov 2007 Week 3, etc. The final report could be labeled Nov 2007 Final, and include data for the entire month. The labels you add will appear in report lists.

Recent Reports of this Type		
<input checked="" type="checkbox"/>	Institution Pa...	Nov 2007 Week 2 Oct 24, 2007 3:56 PM
<input checked="" type="checkbox"/>	Institution Pa...	Nov 2007 Week 1 Oct 24, 2007 3:53 PM

Once the Nov 2007 Final report is available, you could use the delete feature on the Search Results page to delete all of the weekly reports and retain only the month end report.

Search Results			
<input type="checkbox"/>	Report Name	Run Time	Label
<input type="checkbox"/>	Institution Patient Li...	Nov 30, 2007 5:14 PM	Nov 2007 Final
<input checked="" type="checkbox"/>	Institution Patient Li...	Nov 23, 2007 5:06 PM	Nov 2007 Week 4
<input checked="" type="checkbox"/>	Institution Patient Li...	Nov 16, 2007 5:07 PM	Nov 2007 Week 3
<input checked="" type="checkbox"/>	Institution Patient Li...	Nov 9, 2007 5:00 PM	Nov 2007 Week 2
<input checked="" type="checkbox"/>	Institution Patient Li...	Nov 2, 2007 5:05 PM	Nov 2007 Week 1
<input type="checkbox"/>	Institution Patient Li...	Oct 31, 2007 5:12 PM	

Delete Selected Reports Page 1 of 1

If you want to view a list of month-end Final reports only, you can enter the word Final into the **Search** text box.

Search/Sort Criteria			
Search Criteria:			
Report:	<input type="text" value="Institution Patient Listing"/>		
Date Range:	<input type="text" value="10/01/2007"/>	<input type="text" value="12/31/2007"/>	<input type="text" value=""/>
Search Labels and Comments:	<input type="text" value="Final"/>		

Search Results			
<input type="checkbox"/>	Report Name	Run Time	Label
<input type="checkbox"/>	Institution Patient Li...	Dec 31, 2007, 5:01 PM	Dec 2007 Final
<input checked="" type="checkbox"/>	Institution Patient Li...	Nov 30, 2007, 5:14 PM	Nov 2007 Final

For problems or questions, contact the CALGB Help Desk at (877) 442-2542.

To learn how to use the Reporting System, refer to the CALGB Reporting System User Guide, located under the Training Tab on the CALGB Member Site at www.calgb.org.

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2007 Highlights from Some CALGB Committees

Breast Committee

- Published results from comprehensive study of CALGB 8541, 9344 and 9741 in “Toxicity of older and younger patients treated with adjuvant chemotherapy for node-positive breast cancer: The Cancer and Leukemia Group B Experience” (lead author Hyman Muss, M.D.; *J Clin Oncol.* 2007 Aug 20; 25(24):3699-704); study showed that elderly patients treated with newer adjuvant chemotherapy regimens derive the same benefits from newer chemotherapy regimens as younger patients but should be cautioned about the increased risk of toxicity and treatment-related death.
- Developed two preoperative trials (CALGB 40601; CALGB 40603) in women with HER2 positive and triple negative breast cancer.
- Opened CALGB 40302 that will evaluate the role of biologic therapy in combination with hormonal therapy.

Cancer Control and Health Outcomes Committee (CCHO)

- Published “Does health-related quality of life (HRQL) improve for patients who respond to chemotherapy? Analysis of patients with advanced pancreas cancer (APC) receiving gemcitabine on Cancer and Leukemia Group B (CALGB) Study #80303” (lead author Dorothy Romanus, Ph.D.; *Proc Am Soc Clin Oncol.* 2007, Abstract 9008) and “A patterns of care study of post-progression treatment (Rx) among patients (pts) with advanced pancreas cancer (APC) after gemcitabine therapy on Cancer and Leukemia Group B (CALGB) Study #80303” (lead author Deborah Schrag, M.D.; *Proc Am Soc Clin Oncol.* 2007, Abstract 4524).
- Presented third and final analysis from CALGB 70101 at ASCO 2007, which was a series of criterion validation studies to determine the accuracy with which CMS claims measure chemotherapy use and outcomes in elderly cancer patients. This analysis compared CALGB clinical trial data (treated as the gold-standard data source) to CMS claims files for a subset of elderly patients treated on two prior CALGB trials (N=175) and found that CMS claims are only inconsistently valid measures of significant chemotherapy-related toxicity and thus CMS data may not be a good observational data source to use to study chemotherapy toxicity in the elderly.



Committee on Advocacy, Research Communication and Ethics (CARE)

- Completed a multi-center study to evaluate patient perceptions and impact of receiving results from an Intergroup trial (CALGB 49909/N9831); made an oral presentation at the 2007 American Society of Clinical Oncology annual meeting; manuscript in process.
- Established a series of educational forums under the title, “Making Clinical Trials Count for Everyone”; more than 85 people attended the first forum on cultural competency at the summer Group Meeting.
- Helped develop accrual plans for CALGB 40101 and CALGB 90203 that resulted in educational tools for both physicians and patients.
- Manuscript under review on survivor study that identified how patients learn about and enroll in trials.

CRA Committee

- Conducted CRA Orientation Program in fall 2006 in Raleigh, NC; record attendance yielded 113 participants from 60 CALGB institutions; participants completed a prerequisite breast cancer Web-based training module (*see CALGB Member site under Studies/49907 Study Training Page*) and new hire orientation (*see CALGB Member site under Training/Tracked Training/CALGB New Member Orientation*).
- Conducted CRA Continuing Education Program presented to 163 participants at summer Group Meeting; covered topics on molecular markers, their relationship to cancer diagnosis and treatment, and CALGB research (*see CALGB Web site under Meetings/Meeting Presentations tab*).
- Piloted a new, hands-on educational tool (“information kiosks”) at summer Group Meeting; manned by CRAs, Data Coordinators and CALGB staff with laptops, kiosks provided participants with answers to specific questions about audit preparation, CALGB Information Systems, case report forms and long-term follow-up.
- Used new online training system to deliver some educational offerings; more online educational programs are planned in 2008.

— see **A YEAR IN REVIEW**, next page

A YEAR IN REVIEW

GI Committee

- Made presentations at numerous meetings (many internationally) where 15 abstracts were accepted; published 10 papers.
- Published three high-impact colorectal cancer studies, including “Irinotecan, fluorouracil, and leucovorin is not superior to fluorouracil and leucovorin alone as adjuvant treatment for stage III colon cancer: Results of CALGB 89803” (lead author Leonard Saltz, M.D.; *J Clin Oncol*. 2007; 25:3456-3461) and another report from this trial “Association of dietary patterns with cancer recurrence and survival in patients with stage III colon cancer” (lead author Jeffrey Meyerhardt, M.D.; *JAMA*. 2007; 298:754-764), which received widespread media coverage. This study showed that a high fat, western style diet was associated with poorer outcomes in patients with resected colon cancer.
- Published a correlative science paper “The CpG island methylator phenotype and chromosomal instability are inversely correlated in sporadic colorectal cancer” (lead author Ajay Goel, Ph.D.; *Gastroenterology*. 2007; 132:127-38). This paper shows that methylation related gene silencing is likely a more important etiologic event in colon cancer development than was previously appreciated; adding a third pathway to the well described chromosomal instability and microsatellite instability pathways.



GU Committee

- Accepted for publication were two manuscripts on The Men’s Eating and Living (MEAL) Study, which demonstrated that men with prostate cancer are more able than women with breast cancer to change their diet after a 6-month telephone intervention to increase intake of vegetables and fruits and decrease intake of red meats. “The men’s eating and living (MEAL) study: A Cancer and Leukemia Group B pilot trial of dietary intervention for the treatment of prostate cancer” (lead author J. Kellogg Parsons, M.D.; expected to appear in *Urology*) and “Dietary modification in prostate cancer patients on active surveillance: A randomized, multi-center feasibility study” (lead author J. Kellogg Parsons, M.D.; expected to appear in *BJU International*).
- Developed and opened two potentially practice changing studies in clinically localized prostate cancer. CALGB 90203 Randomized phase III study of neoadjuvant docetaxel and androgen deprivation prior to radical prostatectomy versus immediate radical prostatectomy in patients with high-risk, clinically localized prostate cancer (PUNCH Study) opened for accrual last December. The START trial (NCI PR.11/CALGB 140602), A phase III study of active surveillance therapy against radical treatment in patients diagnosed with favorable risk prostate cancer, in collaboration with National Cancer Institute of Canada opened in July.

Leukemia Committee

- Presented by Bayard Powell, M.D., at the 2007 ASCO plenary session were the results of CALGB 9710. This large phase III adult and pediatric intergroup study enrolled 518 previously untreated adults and 64 children (<15 years old) and has changed the standard of care for acute promyelocytic leukemia (APL). The study evaluated the clinical benefit when arsenic trioxide (As₂O₃) is included as the initial post-remission therapy for APL patients in CR1. Overall, the CR rate for both adults and children was 89 percent. Event-free survival was 77 percent at three years on the As₂O₃ arm (median, not reached) compared to 59 percent at three years on the standard arm (median, 63 mos; p=0.0013). Overall, 84 percent of adults were alive at last follow up.
- Published results from CALGB 19801 in “Nelarabine induces complete remissions in adults with relapsed or refractory T-lineage acute lymphoblastic leukemia or lymphoblastic lymphoma: Cancer and Leukemia Group B study 19801” (lead author Daniel DeAngelo, M.D.; *Blood*, Jun 2007; 109: 5136 – 5142). This phase II trial led to the Food and Drug Administration (FDA) approval of nelarabine for patients with relapsed or refractory T-cell acute lymphoblastic leukemia or T-lymphoblastic lymphoma. Nelarabine was administered

— see **A YEAR IN REVIEW**, next page

Leukemia Committee *continued*

on an alternate day schedule (days 1, 3, 5) at 1.5 g/m²/day. The CR rate was 31 percent (95 percent CI: 17-48 percent), and the overall response rate was 41 percent (95 percent CI: 26-58 percent). The one-year overall survival was 28 percent (95 percent CI: 15-43 percent).

- Presented by Jonathan Kolitz, M.D., at 2007 American Society of Hematology (ASH) were data from CALGB 19808, A randomized phase III study of Interleukin-2 for patients less than 60 years old with Acute Myeloid Leukemia (AML) in CR1. A clinical benefit was observed when patients were randomly assigned to receive 90 days of subcutaneous IL-2 at the completion of all planned chemotherapy. By intention-to-treat, for the 214 randomized patients, the three-year disease-free survival rate is 45 percent (95 percent CI: 35-56 percent) on the observation arm and 56 percent (47-67 percent) on the IL-2 arm.

Radiation Oncology Committee

- Played a major role in developing two phase III Intergroup trials that will address the role of high dose radiotherapy in the treatment of lung cancer. CALGB 30609 (RTOG 0617) will test 60 Gy vs 74 Gy conformal radiotherapy in stage III non-small cell lung cancer, and CALGB 30610 will assess three radiotherapy regimens in limited small cell lung cancer and should be activated in early 2008.
- Reported results of the first CALGB brachytherapy trial (CALGB 99809) in "Combination external beam radiation and brachytherapy boost with androgen suppression for treatment of intermediate risk prostate cancer: An initial report of CALGB 99809" (lead author Mark Hurwitz, M.D.). This study assessed brachytherapy in combination with external beam radiotherapy and androgen suppression in intermediate risk localized prostate cancer. Initial results demonstrate the regimen is well tolerated and long-term outcomes are awaited.
- Presented results from CALGB 39904, the first cooperative group trial designed to study radiotherapy in high-risk patients with stage I non-small cell lung cancer. This trial showed that the time to complete a course of definitive radiotherapy could be accelerated to less than 3-1/2 weeks with conformal techniques. An encouraging median survival of 35 months was reported and few severe toxic events were observed.

Surgery Committee

- Activated this year were two new protocols by the Thoracic Surgery and GU Surgery subcommittees: CALGB 140503, A phase III randomized trial of lobectomy vs sublobar resection for small (< 2 cm) peripheral NSCLC study, chaired by Nasser Altorki, M.D., opened in June with an accrual goal of 1,297 patients.



It involves strict quality control for surgeons performing VATS lobectomies, and will determine if wedge resections offer equivalent disease free survival as compared with lobectomies. CALGB 140503 will use a randomization approach where patients are registered prior to surgery but randomized intraoperatively. It is being endorsed by ACOSOG, SWOG, RTOG, and is available through the CTSU.

NCI PR.11/CALGB 140602, A phase III study of active surveillance therapy against radical treatment in patients diagnosed with favorable risk prostate cancer (START), chaired by Adam Kibel, M.D., opened in July. Within CALGB, five member institutions (Roswell Park Cancer Institute, Duke University Medical Center, Washington University School of Medicine and Memorial Sloan-Kettering Cancer Center and University of California at San Francisco) will initially seek to enroll four patients each over 12 to 18 months. If successful, the study will be opened to all CALGB institutions (*see GU Committee section for additional information on page 14*).

- Published "Video-Assisted Thoracic Surgery Lobectomy: Report of CALGB 39802—A Prospective, Multi-Institution Feasibility Study" (lead author Scott Swanson, M.D.; *J Clin Oncol.* 2007; 25:4993-4997) and "Preoperative exercise Vo2 measurement for lung resection candidates: results of Cancer and Leukemia Group B Protocol 9238" (lead author Gregory Loewen, D.O.; *J Thorac Oncol.* 2007 Jul; 2(7):619-25).
- Subcommittees remained active with collaboration between the Breast Surgery Subcommittee and the Breast Committee resulting in the development of two neoadjuvant studies, CALGB 40601 and 40603. Several concepts are in development in the GI Surgery Subcommittee. The Surgical Quality Assurance Subcommittee (SQAC) continues its commitment to surgical excellence in CALGB protocols and due diligence in monitoring surgical studies.

NEWS BRIEFS IN CANCER RESEARCH

Recent CALGB Study Results Show Targeted Therapy May Save Women From Unnecessary Side Effects

Researchers have found they can potentially target chemotherapy for breast cancer to only those women most likely to benefit, sparing the majority of patients from unnecessary side effects.

The Cancer and Leukemia Group B / Breast Cancer Intergroup of North America correlative science study (CALGB 9344) chaired by Daniel Hayes, M.D., clinical director of the breast oncology program at the University of Michigan Comprehensive Cancer Center, found women whose breast cancer expressed a protein called HER-2 were most likely to benefit from adding the drug Taxol to the chemotherapy regimen, while women whose tumors were fueled by estrogen but did not express HER-2 did not get any benefit from the added Taxol. About 15 percent to 20 percent of breast cancers express HER-2, and as many as three-quarters of breast cancers are so-called estrogen-receptor-positive.

“In general, chemotherapy for breast cancer has been a one-size-fits-all approach. Our decision to recommend it is based on whether a woman is at high risk of the breast cancer recurring, without any idea of whether she would benefit from the additional therapy. With this data we hope we will be able to focus chemotherapy on patients whom it’s most likely to help,” Hayes said.

In addition to Hayes, study authors were Donald Berry, Ph.D., from The University of Texas M. D. Anderson Cancer Center; Ann Thor, M.D., from the University of Colorado; Lynn Dressler, Dr.Ph., David Cowan and Susan Edgerton all from the University of North Carolina, Chapel Hill; Donald Weaver, M.D., from the University of Vermont; Gloria Broadwater, Duke University; Lori Goldstein, M.D., from Fox Chase Comprehensive Cancer Center; Silvana Martino, D.O., from the Angeles Clinic and Research Institute; James Ingle, M.D., from the Mayo clinic; I. Craig Henderson, M.D., from the University of California at San Francisco; Larry Norton, M.D., and Clifford Hudis, M.D., both from Memorial Sloan-Kettering Cancer Center; Eric Winer, M.D., from the Dana-Farber Cancer Institute; and Matthew Ellis, Ph.D., from Washington University.

Results of the study appeared in the October 11 issue of the *New England Journal of Medicine* / NEJM. 2007; 357(5):1496-1506.



CALGB Researchers Link Diet with Colon Cancer Recurrence and Death

Patients treated for colon cancer who had a diet high in meat, refined grains, fat and desserts had an increased risk of cancer recurrence and death compared with patients who had a diet high in fruits and vegetables, poultry and fish, according to results from a companion study of CALGB 89903 published in a recent issue of *Journal of the American Medical Association (JAMA)*.

Previous research has indicated that diet and other lifestyle factors have a significant influence on the risk of developing colon cancer. However, few studies have assessed the influence of diet on colon cancer recurrence and survival, according to lead author Jeffrey Meyerhardt, M.D., M.P.H., of the Dana-Farber Cancer Institute.

The companion study examined the influence of two distinct dietary patterns on cancer recurrence and survival in a group of 1,009 stage III colon cancer patients (cancer present in the colon and lymph nodes) enrolled in a clinical trial of postoperative chemotherapy in addition to other treatment. Patients reported dietary intake using a food frequency questionnaire during and six months after supplemental chemotherapy. Two major dietary patterns were identified, prudent and Western. The prudent pattern was characterized by high intakes of fruits and vegetables, poultry, and fish; the Western pattern was characterized by high intakes of meat, fat, refined grains, and dessert.

Patients were followed up for cancer recurrence or death. During a median (midpoint) follow-up of 5.3 years, 324 patients had cancer recurrence, 223 patients died with cancer recurrence, and 28 died without documented cancer recurrence.

Results of the study can be found in the August 15 issue of *JAMA*. 2007; 298(7):754-764.

Irving Berkowitz Remembered



Irving Berkowitz, D.O., Chairman of Hematology Oncology at Metropolitan Hospital and University of Pennsylvania and former Medical Director for the Medical Center of Delaware/Christiana Care, died on November 12.

Berkowitz was a Principal Investigator in clinical cancer research for many national organizations and served on numerous Cancer and Leukemia Group B (CALGB) committees over the past 20 years. He played a key role in the development of the Community Clinical Oncology Program (CCOP) at Christiana Care.

Berkowitz also helped establish a pediatric oncology practice at A.I. duPont Hospital for Children, fulfilling a community need in Northern Delaware. He was a founding board member and medical advisor for the Wellness Community of Delaware. In addition, he maintained a thriving private practice.

Considered a great teacher, Berkowitz was said to have “significantly contributed to setting the standards for quality cancer care throughout the world.”

STAFF UPDATES

@ The Central Office

Michele Sexton joins CALGB as an Administrative

Assistant from SUNY Upstate Medical University where she completed a biological research fellowship. She will support the senior staff and administrative committees. Michelle will also maintain the publications database and track publications for review.

@ The Statistical Center

Lan Lan, Ph.D., joins CALGB as a recently appointed Faculty Statistician from the Duke Clinical Research Institute. She will work with the Leukemia Committee and Cancer Control and Health Outcomes Committee (CCHO). Lan is also an Assistant Professor in the Department of Biostatistics and Bioinformatics at Duke University, and is assigned to the hyperthermia research program at Duke Comprehensive Cancer Center.

As a Staff Statistician, **Jiang Chen, Ph.D.**, will work on pharmacogenetics (WGA and candidate marker) studies with the Pharmacology and Experimental Therapeutics Committee (PET) and analysis of bioinformatics data. Recently, Chen completed a large simulation project for the GU Committee. She brings her talents to CALGB from Duke University where she worked as a researcher.

Faheem Mitha, Ph.D., a new Staff Statistician from the Duke University Laboratory of Computational Immunology (DULCI), joins CALGB with expertise in statistical computation and biological simulation models. Faheem will work with CALGB Information Systems (IS) to develop statistical and computational software for the processing and analysis of bioinformatics data.

QUALITY ASSURANCE

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Training on the New Policy and Procedures

On November 7, 2007, the CALGB Statistical Center held a Webinar to train main and at-large member institutions on the new policy and procedures. The training module from the Webinar is now posted under the Training tab on the CALGB Member Site at www.calgb.org.

Keeping Loss-to-Follow-up Low

Loss-to-follow-up reduces statistical power by decreasing the number of patients for whom an end-point is observed. Importantly, loss-to-follow-up may result in bias in favor of those patients who continue to be followed. Characteristics of patients who are lost-to-follow-up may differ from those that continue to be followed. Also, bias would occur if patients were not lost “at random,” for example, patients were lost due to the toxicity of a regimen.

In addition, imbalances in loss-to-follow-up could occur between or among treatment arms being compared. These sources of bias may affect trial results and impact the validity of a study. Study results may also not be generalizable if loss-to-follow-up is substantial. Thus, efforts should be made to keep loss-to-follow-up low.

PROTOCOL NEWS



BREAST COMMITTEE

OPENED

CTSU— E5103: Dbl-blind dox + ctx -> taxol +/- bevaciz br ca

Study Chair: C. Dang

CTSU— E1105 1st line chemo + trastuz +/- bev HER-2/neu + met br ca

Study Chair: N. Lin

GI COMMITTEE

CLOSED

CTSU—NSABP- C-09: Oxal, cape, flox vs intrv oxal + cape colorectal ca

Study Chair: R. Warren

80603—Ph II SUI1248 in prev pa ca w/ met dis aftr prog on 1st-ln gem tx

Study Chair: E. O'Reilly

LEUKEMIA COMMITTEE

OPENED

I0403—ALL: Phase II study for adolescents and young adults with ALL

Study Chair: R. Larson

LYMPHOMA COMMITTEE

OPENED

50501—Phase II study of bortezomib/lenalidomide in rel/ref mantle cell

Study Chair: V. Morrison

CLOSED

50502—Phase II study of SGN/placebo + GVD for pts with rel/ref CD30+ HD

Study Chair: K. Blum

59903—Hi dose chemo/ASCT vs conv dose CHOP (S9704)

Study Chair: T. Shea

RESPIRATORY COMMITTEE

CLOSED

30501—Induc chemoRT, surg, followed by docetaxel in pancoast tmr (S0220)

Study Chair: A. Lyss

CALGB ASH ABSTRACTS

continued from page 6

>> Transplant Committee

CALGB 109901

Reduced intensity allogeneic transplantation provides high disease-free and overall survival in patients (pts) with advanced indolent NHL and CLL: CALGB 109901.

Shea T, Johnston J, Walsh W, Farag S, McCarty J, Basbey A, Isola L, Stewart M, Kelly M, Owzar K, Linker C for the Cancer and Leukemia Group B, Chicago, IL. [Abstract #486]



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Abbott Laboratories

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The Cancer and Leukemia Group B Foundation is a nonprofit, tax-exempt foundation dedicated to assisting the Cancer and Leukemia Group B – a cooperative group of 29 of the nation's most prestigious medical centers and more than 250 affiliated institutions working together on large-scale clinical trials.

The CALGB Foundation supports the clinical trials and laboratory research of the CALGB and efforts to educate the medical community on methods of cancer diagnosis, treatment and prevention.

Recent initiatives supported by the CALGB Foundation include:

- New chemotherapy treatments for breast, prostate, lung and colorectal cancer.
- New surgical techniques for breast and colon cancer.

- Genetic studies of breast cancer risk.
- Molecular determinants of response to therapy for breast, colorectal and lung cancers, and leukemia.
- Research that improves the quality of life for cancer patients and their caregivers.

Your contribution will support our efforts to find ways to prevent and cure many types of cancer, including leukemia and lymphoma, and cancers of the breast, prostate, lung and GI tract.

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