



CALGB

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Treatments Today*

THE CAL·GAB

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Researching Cancer Control and Health Outcomes in the CALGB

The CALGB Cancer Control and Health Outcomes Committee (CCHO) has been evolving since 1976 when the Psycho-oncology Committee was formed. Some 18 years later, following an NCI mandate for Community Clinical Oncology Program research bases to include cancer control in their institutions' protocols, the Group established the Cancer Control Sciences Committee; the Clinical Economics Committee followed about seven years later. These committees merged in 2001 to form CCHO.

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Cancer and Leukemia Group B

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MESSAGE FROM THE GROUP CHAIR

Moving Forward

The Reason for Group Loyalty



Monica M. Bertagnoli, M.D.

The publication of the Institute of Medicine's recommendations for "A National Cancer Clinical Trials System for the 21st Century" has prompted a great deal of discussion among all stakeholders in the cooperative groups. One aspect in particular has led each of the groups to re-examine its unique contribution to cancer clinical research. In its recommendations for improving the speed and efficiency of clinical trials, the IOM committee recommended consolidation of some "front office operations" of the cooperative group system. By "front office operations" the committee was referring to the activities of the cooperative group scientific committees. These committees provide the forum for multidisciplinary interaction that is required to develop group trials, and as such they are the key feature validating a cooperative group's existence as an independent component of the national cancer clinical trials system.

The implication of this recommendation is that some of the current cooperative groups, particularly those with few disease committees or a single modality focus, will no longer function as independent groups. Currently, there are nine adult cooperative groups and one pediatric group. What would "front office consolidation" mean? Is the best response to the IOM report a change to a system with three or four adult groups and a single pediatric group? Who goes and who stays? Instead of eliminating groups, should some of the groups combine to create a smaller number of new organizations? Reducing the number of groups will undoubtedly lead to increased operational efficiency, but what will be lost with such a move?

CALGB was established in 1956 as one of the first cancer cooperative groups. Fifty-four years later, in June 2010, two founders of the CALGB, Drs. James Holland and Emil (Tom) Frei, were present during the Board of Directors meeting. Among the other board members attending were Dr. Minetta Liu, the current CALGB Principal Investigator at Georgetown University and a former recipient of a CALGB Young Investigator Award; Dr. Clara Bloomfield, who led her first CALGB trial in lymphoma in 1977; and Dr. Stephen Grubbs, representing Christiana Care Health Services, Inc., a CCOP whose accrual to CALGB studies exceeded 320 patients in 2009. These members illustrate that there is a culture in CALGB that successfully supports young investigators, inspires career-long service from outstanding clinician-scientists, and engages a broad research community in our work. In addition, the work of the CALGB is possible because its members advocate for our research in their home institutions. A recent financial analysis, conducted by an independent group at the request of the NCI, found that \$116 million of the total \$361 million yearly cooperative group budget is provided by member institutions, either in the form of cost sharing to support patient accrual or by salary support for CALGB investigators (J.A. Hautala, CTAC, September, 2010).

Why is there such a substantial professional investment in CALGB, extending far beyond what the federal cooperative group awards are able to support? The reason is very simple. As we treat our patients, we all envision ways to make improvements, whether by new drugs, new approaches, or new biological insights. CALGB inspires volunteerism from throughout the broad clinical research community because working together is the only way any of us will make real progress in improving care for our patients. Jim Holland said it best, during a recent discussion of possible changes in cooperative group structure. When I asked him how he would feel if CALGB were to become part of a consolidated group, he responded: *"As long as it helps us get our work done, it's fine with me!"*

CALGB Takes Closer Look at Vitamin D and Cancer Prevention

70806 Vitamin D and breast cancer biomarkers

Despite major advances in early detection and treatment, breast cancer remains a major cause of cancer incidence and death. Improving these statistics can be done through efforts in cancer prevention. Currently, there exist only two agents approved for prevention of breast cancer: tamoxifen and raloxifene. Tamoxifen has been shown to reduce the risk of contralateral breast cancer in women with breast cancer and reduce the risk in women at increased risk.¹⁻³ Raloxifene has been shown to be as effective as tamoxifen in postmenopausal women.⁴ Aromatase inhibitors (AIs) are currently under study, but will only be effective for postmenopausal women.^{5,6} For premenopausal women, the only option is tamoxifen. Additionally, the above agents reduce only estrogen receptor positive (ER+) breast cancer. To date, there are no effective agents known to prevent estrogen receptor negative (ER-) breast cancer.

Tamoxifen use is associated with morbidities including hot flashes, irregular menses, and increased risk of thromboembolic events and endometrial cancer.² Despite the effectiveness of tamoxifen, many women at risk for breast cancer find these morbidities unacceptable and opt not to take tamoxifen.^{7,8} Raloxifene does not appear to cause endometrial cancer, but otherwise is associated with most of the same risks and side effects as tamoxifen.⁴ Aromatase inhibitors have a similar incidence of hot flashes as tamoxifen and raloxifene and are associated with significant arthralgias, atrophic vaginitis and bone loss.⁹ Therefore, in addition to identifying effective chemopreventive agents for ER- disease and premenopausal women, there is also a need for alternative agents that are safe and well tolerated with acceptable side effect profiles. Vitamin D may be such an agent. It is a safe and tolerable supplement with few side effects, and there is mounting evidence for a role in breast cancer prevention. Both laboratory and clinical data have linked vitamin D to breast cancer.

Trial Design

This study is a prospective, double-blinded, randomized placebo-controlled clinical trial for 250 premenopausal

women with increased breast density (greater than or equal to 25 percent of total breast tissue). Women will be randomly assigned to either 2,000 IU of vitamin D or placebo daily for one year. The study will test the effects of vitamin D supplementation on several biomarkers (breast density, serum IGF1, and cellular proliferation (atypia and Ki67)) for one year, evaluate the inter-relationship of these biomarkers, and document the effects of supplementation on serum vitamin D levels and VDR expression. A one-year intervention will minimize unnecessary radiation from mammography (study mammograms will be coordinated with regular annual mammograms) and account for seasonal variation in solar vitamin D by obtaining pre-and post-study mammograms at the same time (season) of the year.¹⁰

This study is of premenopausal women, not only because of their need for chemoprevention options, but also because the evidence suggests a greater effect of vitamin D in premenopausal women. The association between risk and both mammographic density and IGF levels is greatest for premenopausal women: premenopausal women have a greater risk of ER- disease than postmenopausal women, and premenopausal women are less likely to be taking or need calcium and vitamin D supplementation. Women with increased breast density can be readily identified by radiologists, as that density correlates with BI-RADS category 2 and greater. This will allow easy screening of potential patients at the participating institutions.

This study will provide support for use of several breast cancer biomarkers as intermediate markers of breast cancer development and provide the necessary preliminary data for use of vitamin D in larger chemoprevention studies, giving rise to needed options for prevention of ER-disease and greater options for premenopausal women.

Eligibility

Premenopausal women 55 years of age or younger with regular menstrual cycles (at least four cycles in the last six months), and who have a breast density greater than or equal to 25 percent are eligible for the study. Patients who are currently using hormonal contraception should be taking it for at least four months prior to study entry. Those who are taking regular vitamin D supplementation (above 400 IUs daily) and refuse or are unable to stop

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use are not eligible. Women who agree to stop will need to do so for at least six months prior to registration. Patients with a history of breast cancer (including DCIS) or ovarian cancer are not eligible, as are those currently receiving hormone replacement therapy or taking tamoxifen or raloxifene. Women who have taken these medications must have stopped for at least four months prior to study entry. Topical estrogen is allowed. Patients who regularly use oral corticosteroid therapy, lithium, phenytoin, quinidine, isoniazid, or rifampin (all of which can cause vitamin D depletion) are also not eligible.

Refer to the study protocol (CALGB 70806), which can be found on the CALGB Member Web site (www.calgb.org), for complete information on the trial design and patient eligibility.

The Study Chair is Marie E. Wood, M.D., University of Vermont, e-mail: marie.wood@uvm.edu.

References

1. Alkner S, Bendahl PO, Femo M, Nordenskjold B, Ryden L. Tamoxifen reduces the risk of contralateral breast cancer in premenopausal women: Results from a controlled randomised trial. *European Journal of Cancer* 45(14):2496-2502, 2009.
2. Cuzick J, Forbes JF, Sestak I, et al. Long-term results of tamoxifen prophylaxis for breast cancer—96-month follow-up of the randomized IBIS-I trial. *Journal of the National Cancer Institute* 99(4):272-282, 2007.
3. Fisher B, Costantino JP, Wickerham DL, et al. Tamoxifen for the prevention of breast cancer: current status of the National Surgical Adjuvant Breast and Bowel Project P-1 study. *Journal of the National Cancer Institute* 97(22):1652-1662, 2005.
4. Vogel VG, Costantino JP, Wickerham DL, et al. Effects of tamoxifen vs raloxifene on the risk of developing invasive breast cancer and other disease outcomes: the NSABP study of tamoxifen and raloxifene (STAR) P-2 trial. *Journal of the American Medical Association* 295(23):2727-2741, 2006.
5. Cuzick J. Aromatase inhibitors in prevention—data from the ATAC (arimidex, tamoxifen alone or in combination) trial and the design of IBIS-II (the second International Breast Cancer Intervention Study). *Recent Results in Cancer Research* 163:96-103; discussion 264-106, 2003.
6. Richardson H, Johnston D, Pater J, Goss P. The National Cancer Institute of Canada Clinical Trials Group MAP.3 trial: an international breast cancer prevention trial. *Current Oncology* 14(3):89-96, 2007.
7. Port ER, Montgomery LL, Heerdt AS, Borgen PI. Patient reluctance toward tamoxifen use for breast cancer primary prevention. *Annals of Surgical Oncology* 8(7):580-585, 2001.
8. Tchou J, Hou N, Rademaker A, Jordan VC, Morrow M. Acceptance of tamoxifen chemoprevention by physicians and women at risk. *Cancer* 100(9):1800-1806, 2004.
9. Howell A, Cuzick J, Baum M, et al. Results of the ATAC (arimidex, tamoxifen, alone or in combination) trial after completion of 5 years adjuvant treatment for breast cancer. *Lancet* 365(9453):60-62, 2005.
10. Brisson J, Berube S, Diorio C, Sinotte M, Pollak M, Masse B. Synchronized seasonal variations of mammographic breast density and plasma 25-hydroxyvitamin D. *Cancer Epidemiology, Biomarkers & Prevention* 16(5):929-933, 2007.

Trial to Evaluate Upfront Non-Chemotherapy-based Biological Therapy for NHL Patients

50803 A phase II trial of lenalidomide (Revlimid™, CC-5013)(NSC #703813, IND #70116) plus rituximab in previously untreated follicular non-Hodgkin's lymphoma (NHL)

Despite the availability of multiple therapeutic modalities and a high response rate to initial therapy,

most patients with follicular non-Hodgkin's lymphoma (NHL) will develop recurrent or refractory disease and many will ultimately die from lymphoma-related complications.¹ Treatment options have long included chemotherapy and radiation therapy, which have provided clear benefit to patients with these disorders.² Both chemotherapy and radiation therapy, however, also produce irreversible damage to normal tissues that can be manifest in survivors in a variety of ways, including lung and heart disease, infertility and secondary malignancies. The most common treatment-related malignancy in patients treated for NHL is t-MDS/AML, which may develop in up to 10 percent of patients.³

The monoclonal antibody rituximab (directed against the B-cell antigen CD20) was FDA approved based on its activity in indolent NHL, including follicular subtypes.⁴ In 2004, data provided in the National Cancer Institute's SEER program document an improvement in overall survival for patients with follicular lymphoma over the past 20 years.⁵ This improvement is attributable to therapies made available in the last decade, and much of the improvement appears to be due to inclusion of monoclonal antibody-based therapies in standard care.^{6,7} Unfortunately, while chemoimmunotherapy has proved more effective than chemotherapy alone, treatment related malignancies associated with the chemotherapy remain a risk with these treatments, and they are limited in their potential for cure of patients with indolent lymphoma.³

In attempts to avoid or delay the use of chemotherapy in follicular NHL, some investigators have explored regimens in which initial treatment with single agent rituximab is followed by "maintenance" or "scheduled retreatment." These approaches have included additional doses of antibody at regular intervals prior to relapse with both improved response rates and longer time to disease progression than regimens without scheduled retreatment.⁸⁻¹⁰ In addition to chemotherapy, numerous biologic agents are under development and are being evaluated in combination with rituximab in order to explore the possibility of synergistic activity. Phase I or II trials with these agents in combination with rituximab have been developed, and in some cases have demonstrated promising initial results. These combination regimens are particularly attractive to patients and clinicians who wish to avoid toxicities more typically associated with chemotherapy, such as cytopenias, and offer alternative mechanisms of action against chemotherapy-resistant disease.

The activity of lenalidomide against both indolent and aggressive non-Hodgkin's lymphomas, as well its ability to enhance the immune-mediated cytotoxicity of monoclonal antibody therapy and anti-angiogenic effects,

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suggests that the combination of this drug with rituximab might lead to improved responses and long-term outcomes of patients with NHL. Early results of the combination in mantle cell lymphoma are promising, and a phase II randomized trial evaluating the combination of rituximab and lenalidomide compared to lenalidomide alone for patients with relapsed FL is under way in the CALGB, and showing good tolerability. Fowler and colleagues have reported preliminary findings on the combination of lenalidomide and rituximab given on a different schedule in patients with indolent NHL showing good tolerability and promising early response data, with 85 percent overall response rate for evaluable patients.¹¹ Building on the observations that the biological activity of rituximab appears best when given as initial therapy in chemotherapy-naïve patients in an extended induction schedule, and/or when combined with other agents (i.e., cytokines, other antibodies, and/or chemotherapy), this study will evaluate lenalidomide plus rituximab as an upfront non-chemotherapy-based biological therapy for patients with FLIPI low and intermediate risk follicular lymphoma.

Trial Design

The aim of this study is to evaluate lenalidomide plus rituximab as a potential therapy for patients with previously untreated follicular NHL. If the data from this trial provide evidence of efficacy in this patient population, the treatment will be considered for further investigation. A total of 56 patients (50 eligible and evaluable patients) will be enrolled on this trial. The primary outcome of interest is the rate of complete response (CR) as the best-observed response between trial entry and 12 months from enrollment on the trial. Since the treatment period (for observing response outcome) is long, a single-stage design will be used to accrue patients.

Treatment Plan

Patients will receive a total of 12 cycles (administered 21 or 28 days) of lenalidomide and eight doses of rituximab over a period of 12 months, unless either rapid disease progression or unacceptable toxicity is noted.

Eligibility

Patients eligible for this study include those with previously untreated, histologically confirmed follicular lymphoma (WHO classification grade 1, 2, or 3a stage II); low or intermediate risk by FLIPI; no prior systemic therapy for NHL, including chemotherapy or immunotherapy (e.g., monoclonal antibody-based therapy); no known CNS involvement by lymphoma; and no evidence

of active hepatitis B or C infection (i.e., no positive serology for anti-HBc or anti-HCV antibodies). Patients with HIV infection are eligible, provided they meet certain criteria.

Refer to the study protocol (CALGB 50803), which can be found on the CALGB Member Web site (www.calgb.org), for complete information on the trial design, patient eligibility and treatment plan.

The Study Chair is Rebecca Elstrom, M.D., Weill Cornell Medical College, ree2001@med.cornell.edu.

References

1. Johnson, P.W., et al. Patterns of survival in patients with recurrent follicular lymphoma: a 20-year study from a single center. *Journal of Clinical Oncology* 13(1):140-147, 1995.
2. Fisher, R.I. Current therapeutic paradigm for the treatment of non-Hodgkin's lymphoma. *Seminars in Oncology* 27(6 Suppl 12):2-8, 2000.
3. Armitage, J.O., et al. Treatment-related myelodysplasia and acute leukemia in non-Hodgkin's lymphoma patients. *Journal of Clinical Oncology* 21(5):897-906, 2003.
4. McLaughlin, P., et al. Rituximab chimeric anti-CD20 monoclonal antibody therapy for relapsed indolent lymphoma: half of patients respond to a four-dose treatment program. *Journal of Clinical Oncology* 16(8):2825-2833, 1998.
5. Sweson, W., et al. Improved survival of follicular lymphoma patients in the surveillance, epidemiology, and end-results (SEER) program. *Proceedings of the American Society of Clinical Oncology*, 2004.
6. Fisher, R.I., et al. New treatment options have changed the survival of patients with follicular lymphoma. *Journal of Clinical Oncology* 23(33):8447-8452, 2005.
7. Schulz, H., Bohlius, J., Skoetz, N., et al. Combined immunochemotherapy with rituximab improves overall survival in patients with follicular and mantle cell lymphoma: Updated met-analysis results. *Blood* 108a, 2006.
8. Davis, T.A., et al. Rituximab anti-CD20 monoclonal antibody therapy in non-Hodgkin's lymphoma: safety and efficacy of re-treatment. *Journal of Clinical Oncology* 18(17):3135-3143, 2000.
9. Ghielmini, M., et al. Prolonged treatment with rituximab in patients with follicular lymphoma significantly increases event-free survival and response duration compared with the standard weekly x 4 schedule. *Blood* 103(12):4416-4423, 2004.
10. Hainsworth, J.D., et al. Rituximab as first-line and maintenance therapy for patients with indolent non-Hodgkin's lymphoma. *Journal of Clinical Oncology* 20(20):4261-4267, 2002.
11. Fowler, N.H., et al. Lenalidomide and rituximab for untreated indolent non-Hodgkin's lymphoma. *Journal of Clinical Oncology* 27(15s):8548a, 2009.

Bladder Cancer Study to Combine Antiangiogenesis Agent with Standard TCC Therapy

90601 A randomized double-blinded phase III study comparing gemcitabine, cisplatin, and bevacizumab to gemcitabine, cisplatin, and placebo in patients with advanced transitional cell carcinoma

Transitional cell carcinoma (TCC) is the fifth most common new cancer reported in the United States, with an incidence of 67,000 new cases per year, and about 13,000 deaths per year.¹ Seventy percent of TCC are superficial, without invasion of lamina propria or muscle; approximately 30 percent present with invasive or metastatic disease.² Up to 70 percent of patients with superficial TCC recur, and one-third progress to higher grade or stage. Patients with progression to invasive or metastatic disease have poor survival with current therapies. Survival in patients with metastatic or locally

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advanced unresectable transitional cell carcinoma of the bladder is prolonged with cisplatin-based combination chemotherapy. However, durable complete remissions in patients with advanced disease are rare, and median time to progression (TTP) is short. In an updated report of the randomized trial comparing MVAC (methotrexate, vinblastine, Adriamycin® (doxorubicin), and cisplatin) with gemcitabine and cisplatin, survival at five years was 15.3 percent and 13 percent, respectively ($p=NS$).³ These results confirm that TCC is a chemotherapy-sensitive disease, and that improvements in first-line chemotherapy may yield improved progression-free and overall-term survival with this disease. Addition of novel agents to standard chemotherapy may provide such improvements.

Bevacizumab, a recombinant humanized murine monoclonal antibody against VEGF (which plays an important role in TCC progression), has shown significant clinical activity in other cancer types. It has been successfully combined with gemcitabine and cisplatin in other diseases, and proven safe. If the addition of bevacizumab improves progression-free and overall survival, it will change the standard of care in this disease. The phase II study of gemcitabine, cisplatin, and bevacizumab demonstrated a improved median survival of 20.4 months, which compares very favorably to the historical phase III data of 13.8 months, further providing the rationale for this randomized phase III study.

This randomized phase III study will compare standard chemotherapy to gemcitabine/cisplatin and bevacizumab chemotherapy with overall survival as the primary endpoint. It will have early stopping rules for futility of the experimental arm to ensure that excessive numbers of patients are not exposed to an obviously inferior regimen.

Progression-free survival is a secondary endpoint of this study. A non-biased assessment of this endpoint necessitates that this trial be a placebo-controlled, double-blinded study. Previous randomized clinical trials of advanced TCC have treated patients for a maximum of six chemotherapy cycles. Therefore, this trial will allow administration of up to six cycles of chemotherapy. Bevacizumab/placebo as maintenance therapy may be administered until progression for a maximum of two years.

Trial Design

Patients will be randomized in a one-to-one allocation ratio between gemcitabine/cisplatin and bevacizumab,

and gemcitabine/cisplatin and placebo. In the absence of unacceptable toxicity or progression, patients will receive a maximum of six cycles of chemotherapy. If patients do not have disease progression after six cycles, then patients will continue on bevacizumab/ placebo until disease progression or until patients experience unacceptable toxicity. Patients will remain blinded at progression with no crossover permitted. About 500 patients will take part in this study.

Eligibility

Patients eligible for this study include those with metastatic or unresectable transitional cell carcinoma of the urinary tract with progressive metastatic disease or locally advanced disease; no prior combination chemotherapy for metastatic disease; no prior treatment with bevacizumab or other angiogenesis inhibitors; no known brain metastases; no current congestive heart failure; no significant history of bleeding events within six months of registration; and no history of gastrointestinal perforation within 12 months of registration.

Refer to the study protocol (CALGB 90601), which can be found on the CALGB Member Web site (www.calgb.org), for complete information on the trial design, patient eligibility and treatment plan. This study is endorsed by SWOG and ECOG, and open to accrual through the CTSU.

The Study Chair is Jonathan Rosenberg, M.D., Dana-Farber Cancer Institute, jonathan_rosenberg@dfci.harvard.edu.

References

1. Jemal A, Siegel R, Ward E, Murray T, Xu J, Thun MJ. Cancer Statistics, 2007. *CA Cancer Journal of Clinicians* 57(1):43-66, 2007.
2. Cookson MS, Herr HW, Zhang ZF, Soloway S, Sogani PC, Fair WR. The treated natural history of high risk superficial bladder cancer: 15- year outcome. *Journal of Urology* 158(1):62-7, 1997.
3. von der Maase H, Sengelov L, Roberts JT, et al. Long-term survival results of a randomized trial comparing gemcitabine plus cisplatin, with methotrexate, vinblastine, doxorubicin, plus cisplatin in patients with bladder cancer. *Journal of Clinical Oncology* 23(21):4602-8, 2005.

Improving Clinical Trial Accrual for Non-English Speaking Patients

By Sharon G. Levy, R.N.

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One of the biggest challenges we all face is how to increase accruals to our studies. Only three to five percent of adults in the United States who have cancer participate in clinical trials.¹ Of this percent of patients with cancer who participate in clinical trials, collectively less than 10 percent are African American, Asian/Pacific Islander, Hispanic/Latino and Native American. The only way that researchers can learn about potential differences among groups and be able to ensure that study results can be generalized to the population as a whole is to include adequate representation of minorities in clinical trials.

The Coalition of Cancer Cooperative Groups conducted an evaluation of accrual to treatment trials funded by the National Cancer Institute (NCI) from January 2003 to January 2005 in an effort to identify barriers to accrual that need to be overcome. The patient barriers to trial participation that have been identified include: cost/lack of insurance; cultural barriers; lack of awareness; lack of invitation; language/linguistic differences; low literacy; mistrust; practical obstacles such as transportation; and study design/eligibility criteria.

Within the Cancer and Leukemia Group (CALGB), the goal of the Disparities Subcommittee of the Committee on Patient Advocacy, Research Communication, Ethics and Disparities (CARE) is to develop ways to overcome these barriers and to help local sites increase accrual of underserved populations to CALGB studies. While some of the issues faced by our patients are difficult to address at the cooperative group level, such as providing transportation or insurance coverage, one thing we can address is the language barrier for Spanish-speaking patients.

In an effort to start addressing these barriers, the Coalition of Cancer Cooperative Groups is providing funding to translate model informed consent forms into Spanish for all phase III trials listed on the CTSU menu of trials. This should lessen the burden on individual sites translating consent forms. The average cost to translate a consent form is \$1,000 to \$2,000, an expense that the individual institution has to cover. As a result, many institutions simply limit accrual to clinical trials to those who are proficient in English. Ideally, the Spanish language model consents will facilitate increased accrual of Hispanic patients to NCI-sponsored clinical trials. Unfortunately, the informed consent form will not replace the need for a translator while the patient is being seen, in many cases. It still must be documented that the patient understood the information given and had the opportunity to ask questions and have them answered.

While Institutional Review Boards (IRBs) at each individual site have slightly different consent templates and require changes to the model consents, this should provide sites with basic information for translating consents. If your site uses the NCI Central Institutional Review Board as the IRB of record, then the Spanish language consent found on the CTSU Web site will be the same as the CIRB-approved version; and all that has to be done is to add site-specific information. Most IRBs have a short form consent that contains this information already translated in Spanish, and only the PI name and contact information need to be added. It will be necessary to talk with the local IRB about how to integrate basic institutional information found in the short form with the study-specific information in the model consent.

According to the FDA guidelines, if a non-English speaking patient is unexpectedly encountered and an IRB-approved written translation of the consent form is not available, an investigator may enroll a patient using a "short form" written consent document, in a language the patient understands, to document that the elements of informed consent required by 21 CFR 50.25 were presented orally.² Many IRBs require that, in addition to the short form, the patient be given a written summary of the study in a language in which he/she is proficient. The model informed consent form can be used to create this summary.

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ONCOLOGY NURSING PERSPECTIVE

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The table below lists the CALGB studies for which Spanish language model consents are currently available. The goal is eventually to have them available for every phase III study listed on the CTSU Web site. The informed consent forms are updated each time there is a protocol amendment, so sometimes they will be unavailable while the new consent version is being translated. The Spanish language consents can be found on the CTSU Web site under each study, beneath the English consent.

Table I. CALGB Studies on CTSU Menu with Spanish Language Model Consent Forms

CALGB Number	Study Title
10603	A phase III randomized, double-blind study of induction (daunorubicin/cytarabine) and consolidation (high-dose cytarabine) chemotherapy + midostaurin (PKC412) (IND #101261) or placebo in newly diagnosed patients < 60 years of age with FLT3 mutated acute myeloid leukemia (AML)
30506	A randomized phase III trial of adjuvant chemotherapy in patients with early stage non-small cell lung cancer associated with banking of frozen tumor specimens and collection of gene expression profile data
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
30610	Phase III comparison of thoracic radiotherapy regimens in patients with limited small cell lung cancer also receiving cisplatin and etoposide
30801	A randomized phase III double blind trial evaluating selective COX-2 inhibition on COX-2 expressing advanced non-small cell lung cancer
40502	A randomized phase III trial of weekly paclitaxel compared to weekly nanoparticle albumin bound nab-paclitaxel or ixabepilone combined with bevacizumab as first-line therapy for locally recurrent or metastatic breast cancer
40503	Endocrine therapy with or without anti-VEGF therapy: A randomized, 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
40601	A randomized phase III trial of paclitaxel combined with trastuzumab, lapatinib, or both as neoadjuvant treatment for HER2-positive primary breast cancer
50303	A phase III randomized study of R-CHOP vs. dose-adjusted EPOCH-R with molecular profiling in untreated de novo diffuse large B-cell lymphomas
80405	A phase III trial of irinotecan/5-FU/leucovorin or oxaliplatin/5-FU/leucovorin with bevacizumab, or cetuximab (C225) or with the combination of bevacizumab and cetuximab for patients with untreated metastatic adenocarcinoma of the colon or rectum
80702	A phase III trial of 6 versus 12 treatments of adjuvant FOLFOX plus celecoxib or placebo for patients with resected stage III colon cancer
80802	Phase III randomized study of sorafenib plus doxorubicin versus sorafenib in patients with advanced hepatocellular cancer (HCC)
90202	A randomized, double-blind, placebo-controlled phase III study of early versus standard zoledronic acid to prevent skeletal related events in men with prostate cancer metastatic to bone
90203	A randomized phase III study of neo-adjuvant docetaxel and androgen deprivation prior to radical prostatectomy versus immediate radical prostatectomy in patients with high-risk, clinically localized prostate cancer
90601	A randomized double-blinded phase III study comparing gemcitabine, cisplatin, and bevacizumab to gemcitabine, cisplatin and placebo in patients with advanced transitional cell carcinoma
140503	A phase III randomized trial of lobectomy vs. sublobar resection for small (< 2 cm) peripheral non-small cell lung cancer
170601	A phase III double blind trial of oral duloxetine for treatment of pain associated with chemotherapy-induced peripheral neuropathy (CIPN)

References

1. Chistian MC, Trimble EL: Increasing participation of physicians and patients from underrepresented racial and ethnic groups in National Cancer Institute-Sponsored clinical trials. *Cancer Epidemiology, Biomarkers & Prevention* 12(3): 225s-283s, 2003.
2. A Guide to Informed Consent. 11/18/2010. <http://www.fda.gov/RegulatoryInformation/Guidances/ucm126431.htm>

Documentation of Informed Consent

By Debra Herzan, R.N., O.C.N., C.C.R.P.
University of Minnesota

Every clinical trial requires potential participants to sign an informed consent document (ICD) prior to beginning the trial. This regulation is clearly specified in the U.S. Food and Drug Administration (FDA) Code of Federal Regulations (21 CFR 50.20): "... no investigator may involve a human being as a subject in research covered by these regulations unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative ..."

The clinical investigator is responsible for ensuring that informed consent is obtained from each research subject before that subject participates in the research study. The FDA does not require the investigator to personally conduct the consent interview; however, the investigator remains ultimately responsible, even when delegating the task of obtaining informed consent to another individual knowledgeable about the research. It is important that the Institutional Review Board (IRB) be aware of who will conduct the consent interview.

In addition to signing the consent document, the subject/representative should enter the date of signature on the ICD to permit verification that consent was actually obtained before the subject began participation in the study. A copy of the consent document must be provided to the subject and the original signed consent document should be retained in the study records. FDA regulations do not require the subject's copy to be a signed copy, although a photocopy with signatures is preferred, according to the International Conference on Harmonization/Good Clinical Practice (ICH/GCP) guidelines. *(These guidelines relate to an international ethical and scientific quality standard for designing, conducting, recording, and reporting trials that involve human subjects.)*

The consent process does not end with the signing of the ICD. Documentation of the consent process must be included in the patient's medical record (physician's notes, nurse's notes, etc.) and should contain a statement such as "Informed consent was obtained prior to participation in the study." It is not an FDA requirement to also include the time that the subject's signature was obtained. This

medical record documentation requirement has been in effect since 1996.

Many institutions have developed templates for use in electronic medical record systems for documenting the informed consent process. These templates usually contain a field for entering the study identification, dates of participation, contact information for the study principal investigator and subject coordinator (research nurse or CRA), and documentation of HIPAA compliance. Examples of template paragraphs include:

- *The patient was given a copy of the IRB-approved consent form, and all questions were answered before the patient agreed to participate by signing the informed consent document. Informed consent was obtained prior to any study related procedures. A copy of the form was provided to the patient.*
- *The inclusion/exclusion criteria for the protocol were reviewed. The consent form was reviewed, the subject was given ample opportunity to ask questions and all of the subject's questions were answered. A copy of the signed consent form was given to the subject; placed in the subject's chart; placed in the case report form; sent to the Human Studies Subcommittee; and sent to the Investigational Pharmacy. [Note: This example does not contain the sentence "Informed consent was obtained prior to any study related procedures."]*

The template can also include a field for the addition of free text information. This area can be used by the physician or nurse to document eligibility criteria, current medications, performance status, etc.

Does this FDA requirement impact a CALGB audit? The Clinical Trials Monitoring Branch guidelines do not require cooperative group auditors to review the medical record documentation of informed consent. Auditors do check to be sure that the ICD was signed on or before the date of study registration by looking at the date of signature on the ICD. However, medical record documentation is an FDA requirement and is often reviewed by pharmaceutical monitors. This documentation should become a routine part of the informed consent process. For other examples of consent documentation templates, please contact members of the CRA Committee.

Sources

1. FDA: Code of Federal Regulations Title 21, Part 50 Protection of Human Subjects <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRsearch.cfm?CFRPart=50>
2. FDA: A Guide to Informed Consent - Information Sheet <http://www.fda.gov/RegulatoryInformation/Guidances/ucm126431.htm>
3. International Conference on Harmonization: Guideline for Good Clinical Practice: <http://www.ich.org/LOB/media/MEDIA482.pdf>

TRAINING UPDATE

Who to Contact about CALGB Clinical Trials

During the first 90 days on the job, a new clinical research associate (CRA) will receive plenty of resources to help ease the transition. Most likely, this will include mountains of documentation from protocols to policies and procedures, on-the-job training led by a supervisor or a peer, and online training programs such as the CALGB Online CRA Orientation. But what happens when the transition period ends? No matter how comprehensive the 90-day training program was, it is likely that a new CRA will eventually encounter a situation that was not directly addressed in the materials. Prepare for that day by ensuring that all new CRAs know the appropriate person to contact by providing the following list.

Data Coordinator (DC)

Contact the data coordinator for questions about the data submission schedule table in the protocol and how to complete, amend and submit data. Contact information is available on the title page of the protocol and in the directory on the CALGB Member Web site. Search the directory by last name or click the “Whom do I contact in Data Operations” quick link. The main line for Data Operations is 919-668-9355.

Study Chair

Appropriate questions for the study chair include: eligibility*, treatment, dose modifications, and other clinical questions. If you cannot reach the study chair, contact the study nurse or protocol coordinator. Contact information for each person is also available in the CALGB directory and on the title page of the protocol.

*Only the CALGB Group Chair or Executive Officer may approve an eligibility exception. Exceptions are rare.

Pathology Coordinating Office (PCO)

Direct questions regarding sample procurement and sample submission to the Pathology Coordinating Office*. A link to the PCO Web site is available from the CALGB Web site. The PCO Web site does not require a password. You may also reach the PCO by e-mail at path.calgb@osumc.edu, by phone at 614-293-7073 or fax at 614-293-7967.

*Check the protocol for the appropriate contact information if the PCO is not the receiving laboratory.

AdEERS/NCI CTEP Help Desk

A physician is available at 301-897-7494 or AdEERSMD@tech-res.com to answer medical, administrative, and policy questions related to the Adverse Event Expedited Reporting System (or AdEERS). For training or technical issues, call 301-840-8202 or e-mail nciectphelp@ctep.nci.nih.gov.

Cancer Trials Support Unit (CTSU) General Information/Help Desk

Contact the CTSU Help Desk at 888-823-5923 for general inquiries about the CTSU, clinical studies, investigator registration and other issues. It is available 9 a.m. to 5:30 p.m. EST, Monday through Friday (excluding holidays). You may also call this line for assistance* logging into the Oncology Patient Enrollment Network (OPEN) application. *If you need to reset your CTSU Identity and Account Management (IAM) password, go to <https://eapps-ctep.nci.nih.gov/iam/> to obtain a temporary password.

CTSU Central Regulatory Office / CALGB Regulatory Affairs

Contact the CTSU Central Regulatory Office for inquiries about regulatory submissions, Regulatory System Support (RSS) data and compliance. It is the centralized center for the intake, and storage of regulatory documents for all adult NCI-sponsored cooperative group clinical trials. For links to forms and other information, go to https://www.ctsu.org/public/rss2_page.aspx or e-mail CTSURegulatory@ctsu.coccg.org. For regulatory requirements for CALGB trials (such as IRB approvals and required consent forms), contact the CALGB Regulatory Affairs Manager (Andrea Eiring) at 773-702-9814 or andreae@uchicago.edu.

CALGB Help Desk

Contact the CALGB Help Desk to report technical issues with CALGB Web applications (e.g., the CALGB Patient Registration System, Reporting System, Specimen Tracking System) or to activate your account. You may contact the CALGB Help Desk at calgb-support@calgb.duhs.duke.edu or 877-44-CALGB Monday through Friday 8 a.m. to 5 p.m. EST. For 24-hour emergency technical support, call the CALGB Help Desk pager at 888-716-6005. *Note: For password help, the CALGB Help Desk recommends that you first click the “Forgot your password?” link on the application login page and follow the onscreen instructions.*

CALGB Training

For assistance accessing a CALGB online training module, to provide feedback, or to recommend a training topic, contact the CALGB Training Coordinator at 919-668-9343 or CALGBTraining@mc.duke.edu.

CALGB Converts to OPEN System for Patient Registration

Here's great news for institution staff who register patients to CALGB studies! CALGB has converted its first study to accept patient registration from the Cancer Trials Support Unit (CTSU) Oncology Patient Enrollment Network (OPEN) interface. OPEN, which is expected to be used nationwide by cancer cooperative groups in the future, provides a standardized Web-based pre-registration, registration and randomization application for NCI-sponsored studies. As studies are converted, OPEN will replace the CALGB Patient Registration application.

First Up: CALGB Surgical Protocol

On October 1, 2010, CALGB 140503—A phase III randomized trial of lobectomy versus sublobar resection for small (≤ 2 cm) peripheral non-small cell lung cancer became the first CALGB study to go on-line and accept registrations from OPEN. The next CALGB studies to go on-line in OPEN will be 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 and its embedded companions; CALGB 60702—Pharmacogenetic studies in CALGB 30607 and CALGB 70701—Quality of life studies in CALGB 30607. A stand-alone companion (CALGB 70501—Collection of patient-reported symptoms and performance status via the internet) will also receive registrations through OPEN.

In the future, the CALGB will convert all of its studies to use OPEN. To view a listing, log on to the CTSU Member site at <https://www.ctsu.org> and click the OPEN tab. The section entitled “Connect to OPEN” on the resulting page shows protocols currently accepting OPEN registrations.

Accessing OPEN

Institutional staff who want to access OPEN must:

- Have an active CTEP-IAM account. Go to <https://eapps-ctep.nci.nih.gov/iam> and click **Request New Account**.
- Be linked to at least one institution on the CTSU roster or other cooperative group roster.

Registering Patients

If you are a CALGB member, you must have a Registrar role on both the CTSU roster and the CALGB roster. However, if you are currently registering patients through the CALGB Patient Registration System, you should be able to register patients through OPEN without taking further action.

If you are not a CALGB member, you must have a Registrar role on the CTSU roster.

Contact the CALGB Central Office to obtain a Registrar role on the CALGB roster. Contact the CTSU Help Desk at 1-888-823-5923 to obtain a Registrar role on the CTSU roster.

Documentation and Training

CTSU has provided the following documentation and training material for OPEN:

- OPEN Portal Site User's Guide
- OPEN Demonstration Video
- Guidelines for OPEN Access and Crediting
- Frequently Asked Questions

To view the material, go to <https://www.ctsu.org>, log into the CTSU member site, click the OPEN tab, and see the section entitled “Learn More About OPEN.”

CALGB GROUP NEWS

CALGB + NCCTG + ACOSOG = New Collaboration

Collaboration. That was the take-home message from the CALGB 2010 Fall Group Meeting Plenary Session in Miami, FL, in November. Responding to the Institute of Medicine's recent report on cooperative groups, the CALGB began earlier this year to actively seek collaborations that would maximize its ability to achieve its mission – *to conduct clinical studies that lead to the prevention of cancer, identify cures for cancer, or improve the well being of patients living with cancer.*

In June, the CALGB initiated transition to form a joint statistical and data management center with the North Central Cancer Treatment Group (NCCTG) and American College of Surgeons Oncology Group (ACOSOG). In November, the Group sought to explore additional opportunities for mutual benefit between all three cooperative groups. As a result, the three Groups have formed joint statistical and data centers, and will begin hosting joint conference calls and planning meetings for their scientific committees, discussing proposals for shared protocols and other scientific activities.

Moving forward, the aim will be to create a single scientific agenda and consolidate the infrastructure spanning all three cooperative groups. Key to the future success of the CALGB, NCCTG and ACOSOG will be to “understand our strengths and how to preserve them,” according to Monica M. Bertagnolli, M.D., CALGB Group Chair.

A caveat: “We won't achieve our scientific goals unless our studies: activate quickly, accrual rapidly, and run smoothly,” she said. “It will be important to collaborate as widely as necessary to achieve the best science. We must start by asking our members: Who we are? What are our priorities? What important goals can we accomplish together that we could not achieve alone?”

The guiding principles for this collaboration are: best science faster, and actively involving members in the development process for a unified scientific agenda.

The plenary session featured Group chairs from three cooperative groups: Jan C. Buckner, M.D., North Central Cancer Treatment Group (NCCTG); Heidi Nelson, M.D., and David M. Ota, M.D., American College of Surgeons Oncology Group (ACOSOG); and Dr. Bertagnolli. Daniel J. Sargent, Ph.D., CALGB Group Statistician, also addressed attendees.

Merrill Egorin Remembered



Merrill Egorin, M.D., former Vice Chair of the CALGB Pharmacology and Experimental Therapeutics (PET) Committee, and CALGB member for more than 27 years, died on August 7.

Dr. Egorin, an internationally known cancer researcher at the University of Pittsburgh Cancer Institute, served as director of its Clinical Pharmacology

Analytical Facility and co-leader of the institute's Molecular Therapeutics and Drug Discovery Program where he helped develop therapies for cancer patients. His research focused on the pharmacology of cancer drugs -- how to administer them, at what doses and how to combine them with other drugs. The major classes of drugs under study at his laboratory were taxanes, anthracyclines, tyrosine kinase inhibitors, PI3 kinase inhibitors, and heat shock protein 90-interactive agents. Emphasis was on relating the pharmacokinetics and pharmacodynamics of these agents, and on developing novel limited sampling strategies and innovative noninvasive means of assessing drug concentration and drug effect.

He contributed numerous articles to medical journals and was a reviewer or held other editorial positions with many, including the Journal of the American Medical Association and the New England Journal of Medicine. He received scores of awards and honors throughout his dynamic career. Most notably, last year he was awarded the 2009 American ASCO Translational Research Professorship for his work in improving cancer treatments and supporting the next generation of researchers.

New CALGB Appointments

Steven M. Devine, M.D., Associate Professor of College of Medicine at The Ohio State University Medical Center, has been appointed Chair of the CALGB Transplant Committee.

Adam Kibel, M.D., Professor of Surgery, and Holekamp Family Chair in Urology at Washington University in St. Louis; and **Eric Hsi, M.D.**, Section Head of Hematopathology and Medical Director of the Automated Hematology, Flow Cytometry, and Immunohistochemistry Laboratories in the Institute of Pathology and Laboratory Medicine at the Cleveland Clinic, have been appointed to the CALGB Executive Committee.

— see **STAFF UPDATES**, next page

BREAST COMMITTEE

OPENED

CTSUS E3108—A phase II prospective trial correlating progression free survival with CYP2D6 activity in patients with metastatic breast cancer treated with single agent tamoxifen

Study Chair: M. Liu

70806—Vitamin D and breast cancer biomarkers

Study Chair: M. Wood

SUSPENDED

CTSUS S0221—Phase III trial of continuous schedule AC + G Vs. Q 2 week schedule AC, followed by paclitaxel given either every 2 weeks or weekly for 12 weeks as post-operative adjuvant therapy in node-positive or high- risk node negative breast cancer

Study Chair: C. Isaacs

CLOSED

CTSUS ECOG PACCT-1—Phase III randomized study of adjuvant combination chemotherapy and hormonal therapy versus adjuvant hormonal therapy alone in women with previously resected axillary node-negative breast cancer with various levels of risk for recurrence (TAILORx trial)

Study Chair: C. Dees

CCHO COMMITTEE

OPENED

70807—The men's eating and living (MEAL) study: A randomized trial of diet to alter disease progression in prostate cancer patients on active surveillance

Study Chair: J. Kellogg Parsons

GI COMMITTEE

OPENED

80701—Randomized phase II study of everolimus alone versus everolimus plus bevacizumab in patients with locally advanced or metastatic pancreatic neuroendocrine tumors

Study Chair: M. Kulke

SUSPENDED

CTSUS E5202—A randomized phase III study comparing 5-FU leucovorin and oxaliplatin versus 5-FU, Leucovorin, oxaliplatin and bevacizumab in patients with stage II colon cancer at high risk for recurrence to determine prospectively the prognostic value of molecular markers

Study Chair: M. Bertagnoli

CLOSED

CTSUS NSABP-R-04—Phase III randomized study of preoperative chemoradiotherapy comprising radiation therapy and either capecitabine or fluorouracil with or without oxaliplatin in patients with resectable rectal cancer

Study Chair: D. Ryan

CTSUS S0600—Phase III randomized study of irinotecan hydrochloride-based chemotherapy and cetuximab with versus without bevacizumab in patients with metastatic colorectal cancer that progressed on first-line therapy

Study Chair: L. Saltz

GU COMMITTEE

CLOSED

CTSUS E2805—Adjuvant sorafenib or sunitinib for unfavorable renal cell carcinoma

Study Chair: C. Kane

LEUKEMIA COMMITTEE

OPENED

CTSUS E1908—A phase II randomized trial comparing standard and low dose rituximab: Initial treatment of progressive chronic lymphocytic leukemia in elderly patients using alemtuzumab, and rituximab

Study Chair: R. Larson

SUSPENDED

CTSUS E2905—Randomized phase III trial comparing the frequency of major erythroid response (MER) to treatment with lenalidomide (Revlimid) alone and in combination with epoetin alfa (Procrit) in subjects with low- or intermediate-1 risk MDS and symptomatic anemia

Study Chair: A. Artz

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STAFF UPDATES

@ The Central Office

Jennifer Wedgwood, M.S., joins the CALGB as a Protocol Coordinator assigned to the CALGB CCHO and PET committees. She brings to the CALGB her experience as a research lab manager, writing and submitting IRB and protocols, and clinical research.

Kristin Baybayan joins the CALGB as an Executive Assistant, primarily supporting the protocol staff. She recently relocated to Chicago from California where she has worked as a Program Director for a nurse attorney.

@ The Statistical Center

Lynn Werk joins the CALGB as a Clinical Trials Manager. She brings to the CALGB more than 20 years of experience in the pharmaceutical industry from GlaxoSmithKline, along with electronic data capture expertise with the system Inform.

@ Office of the Group Chair

Katherine Faherty joins the CALGB as an Administrative Coordinator. Her responsibilities include coordinating all CALGB meetings and travel, and providing administrative support to the Group Chair and Director of the Office of the Group Chair.

John A. Eldh, M.B.A., brings his experience from Harvard Pilgrim Healthcare, Inc., to the CALGB as a Senior Grants Administrator. He manages the CALGB per-case payment application and payments, along with federal grants for the Office of the Group Chair, financial forecasting, and budgeting.

RESEARCHING CCHO

continued from page 1

Today, the CCHO is chaired by Electra Paskett, Ph.D., Associate Director for Population Science and Professor in the College of Medicine at The Ohio State University Comprehensive Cancer Center, and is comprised of three subcommittees: Health Outcomes, Prevention and Symptom Intervention. The committee aims to conduct innovative scientific studies, including interventional, methodological and health policy research, to reduce the incidence, morbidity, and mortality of cancer in broad populations in the cooperative group setting.

The CCHO has led the field in groundbreaking studies in the areas of quality of life (psycho-oncology), clinical economics and health services, and prevention. Most notable are studies of the effects of cancer diagnosis and treatment on the lives of adult, long-term survivors. In studies of patients treated for Hodgkin disease, 22 percent of long-term survivors were found to have distress sufficient to qualify as a psychiatric disorder. Their post-therapy adaptation was found to be less effective than for adult leukemia patients at a similar stage of follow-up. Nearly 40 percent of patients reported experiencing a conditioned response of nausea and emesis triggered by ambient sensations reminiscent of their treatment.¹⁻³ Additionally, health services researchers within the CALGB have contributed important novel observations in both methodological and empiric research areas. In a study of direct treatment costs associated with participation in approved clinical trials versus non-protocol care in similar settings, there was a minimal 6.5 percent increase in costs generated by study participation.⁴ These data were of substantial use to policymakers considering ongoing support for clinical trials costs as part of the larger national agenda for improving cancer care.

In 1992, CALGB began a seminal study (CALGB 9270—Colorectal adenoma prevention trial using aspirin: A phase III study) of aspirin as an intervention to prevent colon adenoma development in patients with a completely resected colon cancer.⁵ Using a randomized, placebo-controlled, phase III design, patients were assigned to aspirin or placebo and monitored for polyp formation as a part of standard post-surgical surveillance. At a median of 12.8 months after initiating study therapy, 27 percent of the control patients had at least one colonic adenoma documented by colonoscopic biopsy compared to 17 percent of the patients randomized to the aspirin regimen. These data expanded the evidence base supporting the benefit of aspirin therapy as an effective chemoprevention strategy and provided an effective alternative to nonsteroidal anti-inflammatory drugs that carry potential cardiovascular risks.

Active, Recently Completed Research

CCHO investigators demonstrated that women with chemotherapy-induced ovarian failure who receive zoledronic acid (ZA) with their adjuvant chemotherapy for breast cancer have significant ($p < .0001$) less bone loss in the lumbar spine compared to women who do not receive ZA with chemotherapy (CALGB 79809—Phase III trial of intravenous zoledronic acid (Zometa®) (IND# 62751) in the prevention of bone loss in localized breast cancer patients with chemotherapy-induced ovarian failure).

In an National Institutes of Health (NIH) funded case-control study, researchers learned that African-American cancer survivors reported greater satisfaction with their lives and better social support than non-cancer controls, despite the fact that they had significantly more comorbidities, sexual problems and worse physical functioning. Non-cancer controls reported greater hostility toward others and racial discrimination, believe in more cancer myths, had greater mistrust of their physician, and less frequent participation in cancer screening than cancer survivors (CALGB 119901—Quality of life of African-American cancer survivors).

Through comparison of CALGB clinical trial data (treated as the gold-standard data source) to Center for Medicare and Medicaid (CMS) claims files for a subset of elderly patients treated on two CALGB trials (N=175), researchers showed that CMS claims are highly sensitive (>80 percent) and specific (>90 percent) measures of chemotherapy administration, cancer relapse and DFS, but are not valid measures of significant chemotherapy-related toxicity (CALGB 70101—Do Medicare claims measure chemotherapy use and outcomes?).

CALGB 119801—Telephone monitoring: Early identification of psychological distress in cancer patients 65 or more years old during active treatment—tested the value of telephone monitoring in lowering emotional distress and social isolation in older cancer patients with advanced stage disease receiving active treatment. The study showed that patients randomized to the telephone monitoring arm had significantly less anxiety and depression at six months compared to those randomized to the control arm.

Future Research

Initiatives over the next few years will continue to include: assessment of patients' quality of life, with a focus on special populations; interventions to improve quality of life; continued research in developing quality of life and economic analysis measures and functional status assessment; outcomes assessment; symptom intervention; assessment of ways to collect patient-reported outcomes;

— see next page

The following organizations provided support to Cancer and Leukemia Group B research and educational programs in 2010.

INDIVIDUALS

Elizabeth Burton

Martin Edelman

Stephen L. Graziano

Mark Green

Steven Grunberg

Mary & Roger Hecht

Johanna Houseknecht

Wm. Kevin Kelly

John Leonard

Hyman & Loretta Muss

Family Foundation

Rosemary O'Toole

Hank Porterfield

Catherine Quinlan

Susan & Kanti Rai Gift Fund

Elliot & Carol Silverstein

James & Doris Wagner

ORGANIZATIONS

Abbott Laboratories

Abraxis BioScience

Amgen, Inc.

Bayer Healthcare Pharmaceuticals

Breast Cancer Research Foundation

Bristol-Myers Squibb Oncology

Celgene

Genentech BioOncology

Genomic Health

Genzyme

GlaxoSmithKline

Infinity Pharma

Eli Lilly and Company

Millennium Pharmaceuticals

Network for Good

Novartis Oncology

Onyx Pharmaceuticals

OSI Pharmaceuticals

Otsuka Pharmaceuticals

Pfizer, Inc.

Sanofi-Aventis

Sigma-Tau Pharmaceuticals

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prevention using both chemoprevention and behavioral strategies; and economic analyses of clinical treatment trials. The new and continuing protocols conducted by the CCHO Committee will continue to advance health services, quality of life and cancer control research in the cooperative group setting, especially in Community Clinical Oncology Programs (CCOPs).

References

1. Greenberg DB, Komblith AB, Hemdon JE, et al. Quality of life of adult leukemia survivors treated on clinical trials of the Cancer and Leukemia Group B from 1971-1988; predictors of later psychological distress. *Cancer* 80:1936-1944, 1997.
2. Komblith AB, Hemdon J, Zuckerman E, et al. Comparison of long-term psychosocial adaptation of advanced stage Hodgkin's disease and acute leukemia survivors. *Annals of Oncology* 9:297-306, 1998.
3. Komblith AB, Anderson J, Cella DF, et al. Comparison of psychosocial adaptation and sexual function of survivors of advanced Hodgkin's disease treated by MOPP, ABVD, or MOPP alternating with ABVD. *Cancer* 70:2508-2516, 1992.
4. Goldman DP, Schoenbaum ML, Potosky AL, et al. Measuring the incremental costs of clinical cancer research. *Journal of Clinical Oncology* 19:105-110, 2001.
5. Sandler RS, Halabi S, Baron JA, et al. A randomized trial of aspirin to prevent colorectal adenomas in patients with previous colorectal cancer. *New England Journal of Medicine* 348:883-890, 2003.

Cancer Control and Health Outcomes Committee

Chair: Electra D. Paskett, Ph.D., The Ohio State University

Vice Chair: Ann H. Partridge, M.D., M.P.H., Dana-Farber/Partners Cancer Care

Health Outcomes Subcommittee Chair: Ethan M. Basch, M.D., Memorial Sloan-Kettering Cancer Center

Prevention Subcommittee Chair: James R. Marshall, Ph.D., Roswell Park Cancer Center

Symptom Intervention Subcommittee Chair: Charles L. Shapiro, M.D., The Ohio State University Medical Center



2011 CALGB Meetings

Summer Group Meeting

June 23-25, 2011

The Sheraton Boston Hotel
Boston, MA

Spring Committee Meetings*

March 3-5, 2011

InterContinental Chicago O'Hare
Rosemont, IL

Fall Expanded Committee Meetings*

November 17-19, 2011

InterContinental Chicago O'Hare
Rosemont, IL

* Closed meetings open to Cadre members of committee or invited guests.





support **cancer research**
 give to the
Cancer and Leukemia Group B Foundation



The Cancer and Leukemia Group B Foundation, a nonprofit, tax-exempt foundation that raises funds to help the Cancer and Leukemia Group B (CALGB) answer important cancer research questions through large-scale clinical trials. CALGB is a cooperative group comprising 25 of the nation's most prestigious medical centers, 200-plus affiliated institutions and 3,000 medical oncologists and specialists working together to reduce morbidity and mortality from cancer by developing new strategies for the early detection, treatment and prevention of cancer.



By supporting CALGB clinical trials and laboratory research through the CALGB Foundation, you can help find new ways to prevent, treat and cure many types of cancer, including leukemia and lymphoma, and cancers of the breast, prostate, lung and GI tract. Gifts to the Foundation may be designated according to your wishes, and are tax-deductible to the extent permitted by law.



Here are some recent initiatives supported by the CALGB Foundation:

- 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.

Yes! I want to support the Cancer and Leukemia Group B.

Enclosed is my/our contribution of \$ _____ to support the research of the **Cancer and Leukemia Group B.**

- | | |
|--|---|
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| <input type="checkbox"/> In Honor of _____ | <input type="checkbox"/> Please use my gift for the Richard L Schilsky CALGB Achievement Award |
| <input type="checkbox"/> Occasion _____ | <input type="checkbox"/> Please use my gift for _____ |
| <input type="checkbox"/> Please send me information on how to include the Cancer and Leukemia Group B Foundation in my will or charitable trust. | |

American Airlines AAdvantage No. _____
 (Gifts of \$1,000 or more earn 10 miles per dollar donated. Gifts of \$100-\$999 earn five miles per dollar donated. Gifts up to \$99 earn one mile per dollar donated.)

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- Check.** Make check payable to Cancer and Leukemia Group B Foundation.

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Please mail donations to: Sylvia Hrbek, CALGB Foundation, 230 W. Monroe Street, Suite 2050, Chicago IL 60606
 phone (773) 702-9904 / fax (312) 345-0117 / e-mail shrbek@calgb.org