

CALGB

THE CAL·GAB

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QUARTERLY NEWSLETTER OF THE CANCER AND LEUKEMIA GROUP B

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Improving Cancer Care thru Quality Research Data: The Pathologists' Perspective

In the nineteenth century, patient care and human research were two facets of medical science not often spoken together. Fortunately, through the twentieth and into the twenty-first century we have come to realize that the two are inseparable, complimentary, delicately interwoven components of the art and science of medicine. As such, we realize that quality research often results in improved patient care and oftentimes cure.

Quality research is achieved through, among other things, quality information. In Pathology that translates to a correct and reproducible pathologic diagnosis as well as timely accrual and responsible use of appropriate patient material, be it tissue or blood, for prospective as well as retrospective investigation.

The discipline of pathology is as diverse as the physicians who comprise the specialty. As such, there are occasional variations in opinions among pathologists, this is not necessarily a shortcoming. However, we all realize the need for reasonable uniformity and consistency in laboratory diagnosis, especially for the research studies and correlative science projects that depend so much on an accurate and uniform interpretation and confirmatory diagnosis. This defines a major role of the CALGB Pathology Committee.

From the mid 1970's, the explosion of Immunohistochemistry (IHC), In situ hybridization studies, Immunosorbent assays (ELISA, EIA), and gene rearrangement studies have opened new horizons in the field of oncology. From predictors of prognosis and response to therapy, as well as determination of types of treatment options, these ancillary studies continue to slowly unravel the enigma of cancer and represent our most promising tools for the future. Examples such as estrogen and progesterone (hormone) receptor studies and her2/neu in prognostication and



treatment of breast cancer are vital parameters currently considered standard in evaluation and treatment. However, as powerful as the information that these tests provide us is in the fight against cancer, they are delicate and temperamental instruments capable of generating incorrect data if not performed by an experienced scientist in just the right manner.

The multiple steps and pathways involved in obtaining accurate and useful scientific data require intimate involvement with the pathologist and laboratory scientist - from initial diagnosis, tissue procurement and storage, designing and implementing specific studies, to verification and application of the resulting information. Diagnostic verification is the first step. There will always be a need for a single, consistent pathologic diagnosis to verify salient diagnostic information relevant to the needs of particular studies. Timely turnaround of the diagnostic verification process is important to facilitate patient accrual. Submission of diagnostic material, either a paraffin block, unstained slides, or blood samples, is the next important step in the process of obtaining good data. At this point there is a need to insure appropriate quality and quantity of submitted material in order to obtain the best possible information for current as well as future studies. Interpretation of resulting laboratory

MESSAGE FROM THE GROUP STATISTICIAN



Stephen George

Clinical Trials and Public Trust

Stephen L. George, Ph.D.
Director, CALGB
Statistical Center

The primacy of the randomized clinical trial (RCT) as the preferred method for assessing relative treatment efficacy is widely accepted among medical researchers and clinical trialists. No other method can match a RCT in obtaining reliable, unbiased answers to important therapeutic questions. Data mining of large medical databases for nuggets of useful information concerning the effects of therapy, an increasingly common methodology sometimes offered as an alternative to RCTs, is not as reliable as a properly designed and conducted RCT. Most, if not all, of the advances in cancer therapy during the last 40 to 50 years have come from RCTs. Many of these have been conducted by the U.S. cancer cooperative groups sponsored by the National Cancer Institute. Regulatory agencies, most notably the US Food and Drug Administration, require evidence from well-conducted clinical trials for licensing of a new agent or for use of an established agent for a new indication. While the FDA does not insist on RCTs, they are certainly preferred

In addition to the strength of the RCT from a scientific perspective, it has been amply demonstrated that patients enrolled on clinical trials have a more favorable outcome than similar patients not enrolled on trials. This fact is presumably due to better supportive care, closer surveillance, and, when appropriate, the use of the “best known standard” treatment for the control or comparison regimen.

In view of the scientific, medical, and public health importance of RCTs and the benefits for patients enrolled on these trials, it is surprising that so few patients are enrolled on trials. Estimates are that no more than 3% of adult cancer patients in the U.S. receive treatment as part of a clinical trial. The situation is much better in children, with the majority of U.S. children with cancer being enrolled on clinical trials. The dismal state of affairs for adults is due to many factors, among them the lack of appropriate trials for some diseases, overly restrictive eligibility requirements, lack of access to appropriate trials, and patients’ and physicians’ knowledge of and attitudes about RCTs. A recent survey of women with newly diagnosed breast cancer concluded: “Women who had a better understanding of issues about clinical trials had more favorable attitudes toward randomized trials and were more willing to consider partic-

ipation in a clinical trial.” (JCO, 19:3554-3561, 2001) Other studies have found that many potential participants thought that patients on trials were treated as “guinea pigs” and that nothing was known about the treatments to be given.

Such a fundamental lack of understanding of the principles and practices of RCTs threatens to undermine the public trust upon which the future of clinical trials rests. Without this public trust and perceived value, patients will not enroll on clinical trials, and future funding will not be possible. More public education concerning the principles, practices, and benefits of clinical trials are sorely needed. Unfortunately, as recent events have made clear, there are other threats to the enhancement and maintenance of public trust in clinical trials. Among these are failures in oversight of trials, conflicts of interest by participants, and fraud or misconduct.

One major threat to the public trust in clinical trials is the failure to exercise appropriate oversight of trials. Clinical trials are complex endeavors, especially in the



cooperative clinical cancer groups such as the CALGB, where numerous trials and other studies in many different diseases are being managed simultaneously. There are currently 102 active studies open in the CALGB, including 29 randomized clinical trials coordinated by the CALGB or other cooperative groups. In addition, 30 studies have closed within the past year, and 57 studies are in various stages of development. Effective oversight and quality control of these studies are essential. The CALGB has good oversight procedures in place, but we must continue to be vigilant. Violations, or even alleged violations, of these procedures can have extremely negative consequences. The Office of Human Research Protections (OHRP) has temporarily shut down all research involving human subjects at some high profile research institutions because of failure to comply with federal oversight rules, particularly those pertaining to Institutional Review Boards. Most of these suspensions have been based solely upon procedural issues, with no actual harm to patients being alleged, but the most recent episode, at Johns Hopkins, occurred after the death of a healthy volunteer on a study designed to assess lung function in asthma. Another recent episode,

MESSAGE FROM THE GROUP STATISTICIAN

at the University of Pennsylvania, involved the death of a patient on a gene therapy trial. In both cases, there were allegations of improper oversight, failure to follow standard procedures of informed consent, or of inadequate study monitoring, particularly adverse event reporting. Regardless of the merits of the allegations, and however rare they are, they can have devastating effects on public trust.

A second threat to public trust in clinical trials is the real or perceived conflicts of interest on the part of those conducting trials. The potential for problems has increased in recent years with the increasingly complex interactions between academic institutions and corporations, primarily pharmaceutical companies. The CALGB requires disclosure of all potential financial conflicts for CALGB study chairs and others in the Group leadership and reviews these via a standing Conflict of Interest committee on an annual basis. Real or perceived conflicts, financial or otherwise, may lead to suspicions of investigator bias and concerns that patient interests are not the paramount concern of investigators. A series of recent articles beginning in March 2001 in the *Seattle Times* alleged that key investigators in a clinical trial conducted between 1981 and 1993 not only failed to follow established policies and procedures, but received major personal financial incentives, including stock options, from the sponsoring company. Again, regardless of the merits of these allegations, the damage to public trust is enormous.

A third threat to public trust is the rare, but continuing, occurrence of scientific misconduct or outright fraud. Most researchers believe such episodes are extraordinarily rare, given the large numbers of clinical trials, but they do occur, and with distressing regularity. The effect of misconduct or fraud on public trust is usually far greater than any real effect on the scientific process or on the safety of individual patients. In the early 1990s, it was discovered that a single investigator in the NSABP had fraudulently altered eligibility data on some patients entered on important breast cancer trials from 1977 to 1990, including the definitive lumpectomy trial (*Chance*, 10:3-5, 1997). It was immediately clear that such falsification, involving a small percentage of patients and coming from a single investigator, could not have affected the scientific conclusions from the involved studies, but the public furor was immense and damage to public trust incalculable. In a recent case, a South African investigator falsified data on a high profile trial involving high dose chemotherapy in breast cancer patients (*JCO*, 19:2771-2777, 2001). This was a more serious case because of the more extensive nature of the fraud, and because it was from a study conducted by a single institution. One of the strengths of multi-institutional trials such as those conducted by the CALGB is that no single institution is dominant. Unfortunately, these are not completely isolated episodes. A recent paper from researchers in Germany described the dramatic therapeutic effect of a cancer vaccine against advanced renal cell carcinoma, a

notoriously difficult clinical setting (*Nature Medicine*, 6, 332; 2000). Such a finding is of major importance in this disease. Unfortunately, questions have arisen both about the vaccine and the results, and there is now an ongoing investigation of scientific misconduct in Germany. In the U.S., the Office of Research Integrity has a steady stream of investigations active at all times. For example, in 1999, 72 institutions reported misconduct activities to the ORI. Regardless of the rarity of these episodes, and of the truth of the allegations, the cumulative effect on the public trust is incalculable.

It is imperative to all of us involved in clinical trials to recognize that we have an obligation to do all we can to maintain and enhance the public trust upon which future progress depends. This obligation requires us to be active in public education, to adhere to oversight policies and procedures, to be sensitive to potential conflicts of interest, and to follow the highest ethical standards in the design, conduct, analysis, and reporting of results. To do otherwise jeopardizes the entire clinical trial enterprise.



IMPROVING CANCER CARE THRU QUALITY DATA CONTINUED

data is the next step in which the laboratory scientist is involved. Verifying data and confirming hypotheses are among the most important roles that the pathologist and laboratory scientist undertake in the process of clinical investigation. Finally, designing future studies with the use of banked material from prior investigations offers an invaluable opportunity for both clinical and laboratory researchers to tap into the resources of ongoing or completed clinical studies, some with large accruals, as well as long and detailed follow-up data.

The value of archived tissue bank material is well known and laboratory scientists are finding new ways to preserve as much of this irreplaceable and limited resource as possible. From the use of double immunolabeling studies to tissue microarray analysis, new methods to conserve resources are a paramount priority. Tissue microarray technology incorporates literally hundreds of patient specimens onto one or two reprocessed paraffin blocks instead of the hundreds upon hundreds of slides and blocks used currently. This technology saves precious and expensive antibodies as well as one-of-a-kind specimens. Although initially labor intense, microarray technology affords researchers the opportunity to evaluate multiple markers in a cost efficient and timely manner. It also allows scientists the opportunity to greatly expand the scope of any study design. This pioneering technology is currently available to the CALGB at our Pathology Coordinating office, its use in future studies is already planned.

The CALGB is at the forefront of tissue procurement and banking, taking a proactive role and providing the necessary resources to insure its success. The leadership of the Group established a procurement and storage facility long before it was generally accepted as the thing to do. Starting with the close and custodial care of Dr. Maurice Barcos, filling all his available space at Roswell Park Cancer Center in Buffalo, New York, the leadership at CALGB has continued and expanded its commitment to this endeavor with the establishment of the Pathology Coordinating Office (PCO) at Ohio



State University. This office is responsible for proper retrieval, storage, distribution, and use of banked material, helping to insure the highest quality of resulting data from both prospective and retrospective studies. Because of the delicacy and intricacy of many of the current studies using banked material, we recognize the need for proper cataloging, optimal storage, and correct categorization of this valuable resource. Viability of a specific test or assay is often dependent on adequate fixation and storage as well as proper antigen retrieval. The PCO oversees the proper procurement, maintenance and processing of quality material to insure that results are of the highest quality. Pathologists specifically assigned to study protocols to insure quality control and quality assurance check the quality of the product provided by the PCO. Finally, after careful and meticulous checks are performed, the material is sent to the appropriate investigator. This process is a shared responsibility, not only by the PCO and the Pathology Committee, but also by clinicians and laboratory professionals at contributing institutions.

The CALGB leadership is committed to expanding the role of the Pathology Committee, recognizing the need for correlative science projects in addition to the ongoing clinical trials. It has already demonstrated its support by contributing resources to this process and listened to the needs of the pathology group, helping with recruitment of a host of respected leaders in subspecialties of pathology. It continues to bring together dedicated laboratory physicians willing to volunteer their time and energy.

Success will be insured with this dedicated cadre of pathologists and the continuing support of CALGB. Together, quality research data will be achieved and the ultimate beneficiary will be the patients whom we are collectively committed to serve.

*Jonathan F. Lara and Carolyn Compton
for the CALGB Pathology Committee*

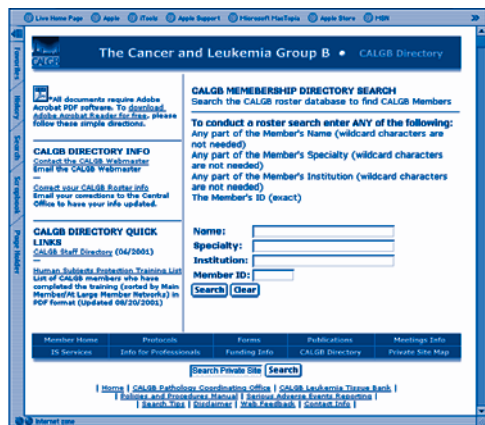
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CALGB GROUP NEWS

CALGB Web Stats

From December 1, 2000 to August 21, 2001 15,548 separate individuals have visited the CALGB web site. 6,438 have returned to the site one or more times.



On average, 1,495 CALGB web pages are looked at every day.

The average user spends 3 minutes and 9 seconds at the CALGB web site and looks at between 2 and 3 pages.

The five most downloaded documents from the CALGB website are:

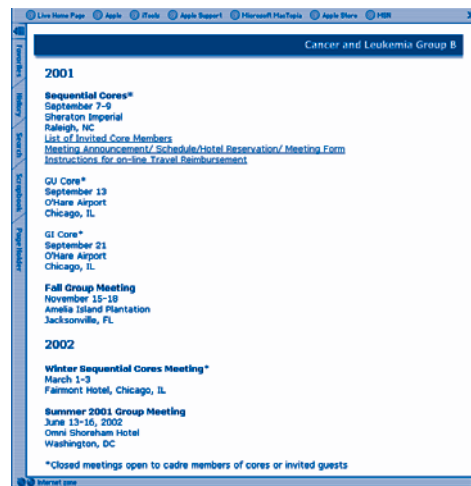
1. Summer 2001 Group Meeting Booklet
2. March 1-4, 2001 Core Meeting Information
3. September 8-10, 2000 Core Meeting Information

Medwatch Forms

The CALGB Central Office must receive a copy of all FDA Medwatch forms (3500) submitted to the FDA for CALGB studies. Although the FDA Medwatch form is now available electronically via links from the NCI Adverse Event Expedited Reporting System (AdEERS) website, the CALGB Central Office is unable to receive these reports electronically. It is very important that the CALGB Central Office be copied on all serious adverse events for CALGB studies sent to the FDA. If you have any questions regarding this, please call Gabrielle Dye, Assistant Regulatory Coordinator at 773-834-2545 or send an e-mail to calgb@uchicago.edu.



4. Staff Directory
5. Human Subjects Protection Training: List: individuals who have completed the training by institution



Group Changes

Principal Investigators:

At Rhode Island Hospital **William Sikov MD** is the new PI, taking over from Louis Leone, MD.

'e' communication

Your email address is a vital connection between you and the CALGB.

Members with valid email addresses will be able register on-line for the **CALGB Fall Group Meeting** in Florida from mid-September.

Make sure your correct email address is part of your profile in the CALGB member database. Send corrections or updates to gdy@midway.uchicago.edu

The CAL•GAB is published quarterly by the Cancer and Leukemia Group B and is distributed free to the CALGB active membership. Suggestions for articles are encouraged. The next **copy deadline is November 12**, for the Winter 2001 edition.

Articles and correspondence should be directed to: Anne Battershell, CALGB Publications Coordinator at — abatters@uchicago.edu or at 208 S. LaSalle St., Suite 2000, Chicago, IL 60604-1104 Voice: (773) 702-9479 Fax: (312) 345-0117

PLEASE NOTE: While we make every effort to provide accurate dosing information in the CAL•GAB, you should always check the appropriate drug dosages before prescribing and/or administering any medication.

Treating CML at the molecular level

Chronic Myeloid Leukemia (CML) is a disease of the myeloid stem cells. It was first described in the literature in 1845. CML differs from all other leukemias in that it is directly caused by the reciprocal translocation of the long arms of chromosome 9 and 22. This landmark discovery of the Philadelphia Chromosome (Ph+) took place at the University of Pennsylvania in 1960. Since then, genetic karyotyping of leukemias has become standard care. Ninety-five percent of all CML patients exhibit the Philadelphia Chromosome (Ph+).

The reciprocal translocation of these chromosomes creates a fusion protein called Bcr-Abl. This protein has tyrosine kinase activity which has been postulated to be responsible for the transformation to CML. The result is a marked increase of the erythroid (red blood cell line), granulocytic (white blood cell line), and megakaryocytic (platelets) progenitor cell lines as well as a decreased ability for cell regulation, seen in the chronic phase. Eventually the leukemic cells lose their ability to differentiate, making the bone marrow hypercellular.

CML is a disease of middle age, with the largest percentage of patients presenting during their 50's, however, it is also known to occur both in younger and older ages. A slightly increased number of males compared with females will be diagnosed with CML. It has three well-documented phases:

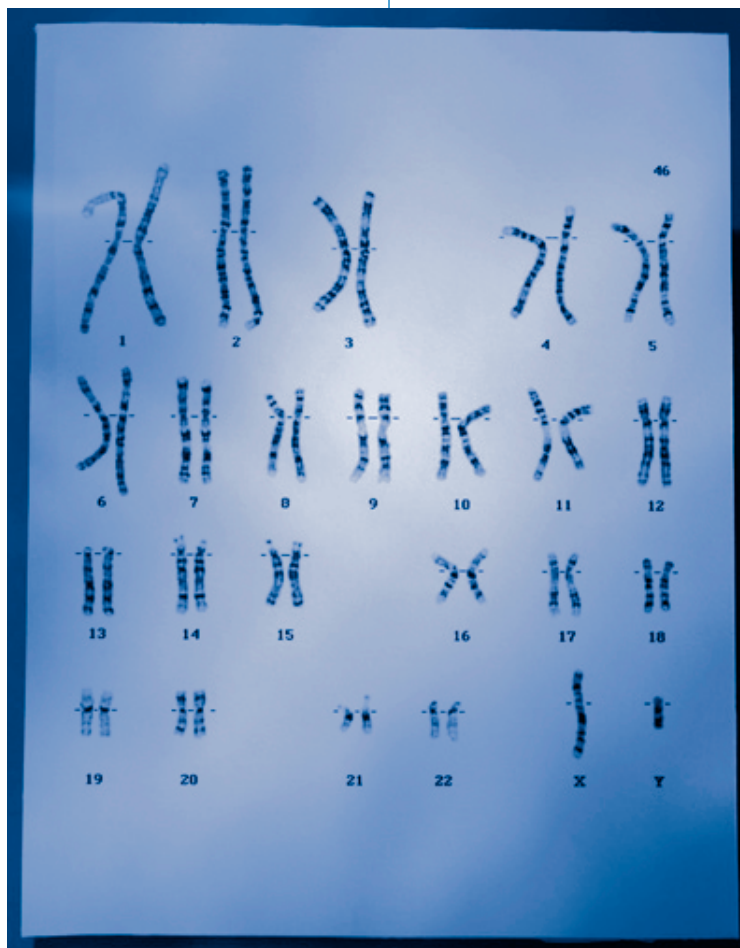
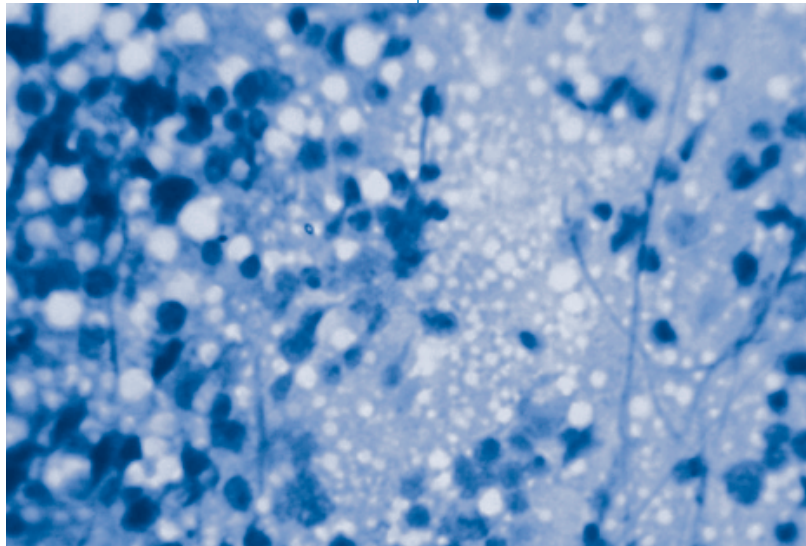
1) chronic phase-which is considered an indolent phase, has a median duration of approximately 3-4 years. Patients can present with: moderate to severe left upper quadrant pain (as a result of splenomegaly),

splenic infarction (caused by granulocyte congestion that jeopardizes splenic circulation), friction rub (heard over the spleen and increased with respirations) worsening anemia, hepatomegaly, sternal tenderness, increase in numbers of basophils, eosinophils, and platelets, as well as a decrease in leukocyte alkaline phosphatase (LAP).

2) Accelerated phase-which can last from 3-9 months .

This is a more aggressive phase where the patient will have complaints of increasing fatigue, anemia, bruising, and bleeding, weight loss, night sweats, possible bone pain, worsening abdominal discomfort, increased hepatosplenomegaly, and possibly the formation of chloromas (nodular tumors of the skin). This phase is increasingly refractory to treatment; 3) Blast crisis is the terminal phase and may be 3-6 months in duration. This phase is very similar to an acute leukemia with severe symptomology and extreme susceptibility to infections and hemorrhage.

Chronic phase therapy consists of hematologic control to keep cell counts under control for as long as possible, thus hoping to delay progression of the disease. Hydroxyurea, busulfan, interferon- α + Ara-C, are the current standard drug therapies. Interferon- α has been shown to prolong survival when compared to hydroxyurea alone. However, these treatments do nothing to offer an actual cure for the disease and have an array of what can be severe side effects and toxicities. Allogeneic bone marrow transplants have the potential for curing the disease but are only an option for 20% of this population due to the absence of compatible donors and/or age restrictions. As CML progresses, it becomes more and more refractory to treatment.



Treating CML at the molecular level

Gleevec[®], (STI-571) is a new type of antiproliferative agent known as a signal transduction inhibitor (or STD) which stops the signal being transmitted by the abnormal oncogene, Bcr-Abl. STI-571 specifically inhibits the tyrosine kinase activity of Bcr-Abl resulting in decreased proliferation of hematopoietic stem cells. Gleevec is known to molecularly target primarily abnormal tyrosine kinases, such as BCR-ABL, thus preventing the enzyme from stimulating the over production of the leukemic cell line, while allowing normal stem cells to proliferate and repopulate the bone marrow. Gleevec has been demonstrated to not only normalize the blood counts and appearance of the bone marrow in patients with CML (hematologic remission), but to also decrease the number of abnormal cells detectable by cytogenetic testing (cytogenetic remission). In some patients, there were no abnormal cells detectable by standard cytogenetics after two months of therapy. However, because Gleevec is a new therapy, there are only short-term results. It remains to be determined how durable hematologic and cytogenetic remissions will be.

Gleevec is given orally, at a beginning dose of 400mg/day. The dose can be escalated up to 800mg/day, if required. It is important to have the patient take Gleevec with a full 8 ounce glass of water and a full breakfast. There have been minimal side effects that include nausea (decreased when Gleevec is taken with a meal), myalgias, edema, and diarrhea. Even with the administration of 800 mg/day, the majority of adverse events seen have been only grade 1 (mild) or grade 2 (moderate). It is essential, however, that the patient not take any over the counter or prescription medications which include acetaminophen, or drugs known to be metabolized by CYP450 isoenzymes. These drugs, when taken at the same time as Gleevec, can cause severe liver toxicity and possibly death. Strict observation of daily weights is also required to ensure the quick identification of any edema or weight gain which may require the addition of diuretics.

Gleevec has also shown antiproliferative activity in treating cancers which exhibit tyrosine kinase activity related to c-Kit and platelet derived growth factor (PDGF). These tyrosine kinases are found in certain GI stromal, small-cell lung, prostate and cerebral tumors. This information will make several new trials in cancer research available. CALGB 80004, STI-571 for Gastrointestinal Stromal Tumors was activated on

January 1, 2001. CALGB 10001 is a pending trial for ALL treatment with STI-571. There is also serious discussion of STI-571 trials being made available through CALGB in small-cell lung, and prostate cancer.

Mary Abraham

Nurse Liaison To The CALGB Leukemia and Leukemia/Lymphoma Correlative Science Committees
SUNY Upstate Medical University, Regional Cancer Center,
Syracuse, New York.

thanks to Stephen Graziano, M.D. and David Grinblatt, M.D.
for their input



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CLINICAL CANCER TRIAL NEWS

Coalition Announces New Clinical Trial Tool - TrailCheck TrialCheckSM

The Coalition of National Cancer Cooperative Groups is proud to unveil TrailCheck TrialCheckSM.

TrialCheckSM is a new database technology that allows physicians, nurses, clinical researchers and practice managers an easy-to-use clinical trial search tool for patient matching of to screen patients for cancer clinical trials and will be available soon.

The Coalition invites cooperative group members to visit www.TrialCheck.org and register for password access.

TrialCheckSM allows members users the ability to quickly query and screen a database of over approximately 300 current cCooperative Ggroup clinical trials, including all of CALGB's active trials. The database contains all the trials of the cooperative groups that are members of the Coalition.

Clinical trial results that match the user's request are available in only seconds in a printer-friendly version. Other valuable information about the clinical trials includes the abstract and eligibility document when that information is available, as well as a list of participating institutions. In addition, TrialCheckSM gives users the ability to search by institution and by physician name.

"We created TrialCheckSM as a tool for in our continuing efforts to increase accrual of patients to cancer clinical trials. We're encouraging physicians to use TrialCheckSM and accept encourage the consideration of clinical trials as the standard of care and an integral part of patient care," said Robert L. Comis, M.D., President of The Coalition of National Cancer Cooperative Groups. "The tool is designed to provide physicians and their staffs with fast and efficient access to cooperative group trials."

Over the last 25 years, cooperative group studies have been responsible for many of the major discoveries in cancer therapies. Unfortunately, there is a shortage of participants in these trials - one reason being that there is no fast, easy way for physicians or their staff to find appropriate clinical trials for patients. The Coalition has developed this new web-based technology tool that will allow members to quickly and easily determine identify potential which clinical trials for which a patient may qualify to participate in.

Visit TrialCheckSM at www.TrialCheck.org and register for a password.

or fFor more information email the Coalition at feed-back@trialcheck.org.

NEW CANCER TRIALS HELP WEBSITE OFFERS TOOLS, INFORMATION TO BOLSTER CLINICAL TRIALS ENROLLMENT

PHILADELPHIA - An important new tool in efforts to double the numbers of participants in adult cancer clinical trials has debuted on the Internet - Cancer Trials Help.

The site, at <http://www.cancertrialshelp.org>, was developed by the Coalition of National Cancer Cooperative Groups, a leading national voice for cancer clinical trials. It was designed by VirTu, a Philadelphia-based strategic integrated marketing agency.

"Right now, only about five percent of adult cancer patients in the U.S. participate in clinical trials," said Robert Comis, M.D., a Philadelphia oncologist and president of the Coalition. "Our goal is to double that number over the next five years, and Cancer Trials Help is a key facet of that effort."

Recognizing the Coalition's diverse audiences, Cancer Trials Help has subsections targeted at the needs of health-care professionals, Coalition members, patient advocates and patients/families/caregivers. Its features include:

- A list of available trials being conducted by the seven cooperative groups which are members of the Coalition.

- The Clinical Trial ABCs, an introduction to the subject written for a patient and family audience.

- Information on Coalition programs for health professionals

- The Patient Advocate Toolbox, including profiles of all 26 patient advocate groups which are Coalition members.

The site launch was timed to coincide with publication of "Cancer Clinical Trials: Are They Right for You?" a special advertising section in the May 7, 2001 edition of Newsweek. Visitors can download or request hard copies of the section.

Clinical Trials Help goes well beyond the insert, which is primarily targeted toward patients and the public, noted Joseph F. Barone, president, VirTu. VirTu and the Coalition are already involved in the planning for Phase II of the site, expected later this year.

The Coalition works to improve access to clinical trials; to develop and manage new trials; to improve health and economic outcomes; and to be involved internationally in the field of cancer research. Members of the Coalition include cooperative groups, patient advocate organizations, and cancer research and treatment centers.

VirTu is an integrated strategic marketing company that has been building Web sites and creating Internet-based marketing solutions since 1996. Its clients include CIGNA Group Life, Penn Mutual Life Insurance Company, Deloitte Consulting and the e-Philadelphia Technology Alliance. For more information on VirTu, visit <http://www.virtuinc.com>.

Joe Barone, 215 790-3250

CALGB INVESTIGATOR AWARDS

Cancer Research Grants for CALGB Oncology Fellows 2001 Recipients

*Richard L Schilsky MD, CALGB Chairman presenting the 2001 Investigator Awards
at the June 2001 Group Meeting in Ottawa*

Corey Cutler,
Dana-Farber
Cancer
Institute



Manish
Arvind
Shah
Memorial Sloan-
Kettering
Cancer Center



Jonathan
D'Cunha,
University of
Minnesota
with Dale Pike
of Pharmacia
Corporation



Hsingjin Liu,
University of
Minnesota



not pictured Claudio G. Brunstein,
University of Minnesota



PROTOCOL NEWS

CANCER CONTROL & HEALTH OUTCOMES

NEW

70004—L-Selenium-based Chemoprevention of Prostate Cancer among Men with High Grade Prostatic Intraepithelial Neoplasia *Study Chair: W. Robert Lee MD*

119802—Fluoxetine in Stage IIIB/IV Non-small Cell Lung Cancer (NSCLC): A Limited Access Phase II Pilot Study to Improve Quality of Life During Chemotherapy *Study Chair: Donna Greenberg, MD*

GI COMMITTEE

NEW

89903—Sequential Phase II Study of Anti-idiotypic Monoclonal Antibody Vaccine that Mimics CEA in Patients with Minimal Metastatic Colorectal Carcinoma *Study Chair: Mitchell Posner, MD*

80002—Local Excision Alone or Local Excision Plus Adjuvant Chemoradiation Therapy For Small Distal Rectal Cancers *Study Chair: Ronald Bleday, MD*

GU COMMITTEE

NEW

90006—A Phase II Study of Estramustine, Docetaxel, and Bevacizumab (anti-VEGF Antibody) in Men with Hormone Refractory Prostate Cancer *Study Chair: Joel Picus, MD*

CLOSED

9782—A Phase II Trial of Potency-Sparing Hormonal Therapy in Patients with Elevated Serum PSA after Radiation Therapy or Radical Prostatectomy for Prostate Cancer *Study Chair: Joel Picus, MD*

99813—A Phase II Study of Estramustine, Docetaxel and Carboplatin with G-CSF Support in Men with Hormone Refractory Prostate Cancer *Study Chair: William Oh, MD*

99901—A Phase II Study of 9 Nitrocamptothecin (9-NC, IND # 60,162) for Hormone Refractory Prostate Cancer *Study Chair: Edward Gelman, MD*

99908—Phase III Trial of Methotrexate, Vinblastine, Doxorubicin and Cisplatin vs. Carboplatin and Paclitaxel in Advanced Carcinoma of the Urothelium *Study Chair: Martin Edelman, MD*

LEUKEMIA COMMITTEE

NEW

19902—CMA-676 With and Without Chemotherapy for Patients With Refractory/Relapsed Acute Myeloid Leukemia: A Phase IIb Randomized Study *Study Chair: Richard Stone, MD*

LYMPHOMA COMMITTEE

NEW

59909—A Phase II Study of Intensive Induction Chemotherapy Followed by Autologous Stem Cell Transplantation Plus Immunotherapy for Mantle Cell Lymphoma *Study Chair: Lloyd Damon, MD*

50002—A Phase II Trial of Thalidomide (NSC 66847, IND 48832) for Patients with Relapsed or Refractory Low Grade Non-Hodgkin's Lymphoma *Study Chair: David Grinblatt, MD*

CLOSED

9793—A Phase III Trial of CHOP versus CHOP and Chimeric Anti-CD20 Monoclonal Antibody (IDEC-C2B8) in Older Patients with Diffuse Mixed, Diffuse Large Cell and Immunoblastic Large Cell Histology Non-Hodgkin's Lymphoma *Study Chair: Vicki Morrison, MD*

MELANOMA WORKING GROUP

NEW

500002—Phase III Trial of High Dose Interferon Alpha 2b vs Cisplatin, Vinblastine, DTIC, plus IL 2 and Interferon in Patients with High Risk Melanoma *Study Chair: Frank Haluska, MD*

PHARMACOLOGY & EXPERIMENTAL THER

CLOSED

9863—Phase I Study of Irinotecan (CPT-11, NSC # 616348) in Patients with Abnormal Liver or Renal Function or with Prior Pelvic Radiation Therapy *Study Chair: Alan Venook, MD*

RESPIRATORY COMMITTEE

NEW

30002—Paclitaxel/Topotecan/Etoposide Induction Followed by Consolidation Chemoradiotherapy for Limited Stage Small Cell Lung Cancer : A Phase II Study *Study Chair: Antonius Miller, MD*

30101—A Phase II Study of ZD1839 in Patients with Malignant Mesothelioma *Study Chair: Ramaswamy Govindan, MD*

CLOSED

9732—A Randomized Phase III Study Comparing Etoposide and Cisplatin with Etoposide, Cisplatin, and Paclitaxel in Patients with Extensive Small Cell Lung Cancer *Study Chair: Harvey Niell, MD*

39802—Video-assisted Lobectomy for Peripheral (≤ 3 cm) N0, Non-small Cell Lung Cancer: A Phase II Feasibility Study *Study Chair: Scott Swanson, MD*

SOLID TUMOR CORRELATIVE SCIENCES

CLOSED

8869—Laboratory Studies in Breast Cancer Tumor Tissue *Study Chair: Hyman Muss, MD*

ADDITIONAL FUNDING FOR CALGB STUDIES

Supplemental support is available to qualifying institutions for participation in these studies. For more information, visit the CALGB website or contact Mary Sherrell, Financial Officer at (773) 702-9856.

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

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

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

9763—Prospective evaluation of body surface area as a determinant of paclitaxel pharmacokinetics/pharmacodynamics in women with solid tumors

9872—Activated protein C resistance and tamoxifen-associated thrombosis

19902—CMA-676 +/- Chemo for Refractory/Relapsed AML

39803—Pre-resectional minimally invasive surgical restaging of stage III (mediastinal node positive) non-small cell lung cancer (NSCLC)

49805—Phase III randomized double blind study of letrozole v. placebo in women with primary breast cancer completing 5+ years of adjuvant tamoxifen

49808—A 2x2x2 Factorial Phase III Study of Multimodality Therapy for Stage III Breast Cancer Comparing 4 Cycles of AC With or Without Dexrazoxane Followed by 12 Weeks of Single Agent Paclitaxel with or without Herceptin Followed by Local Therapy and 40 Weeks of Weekly Herceptin Or None

59903—Randomized phase III trial comparing early high dose chemoradiotherapy and autologous stem cell transplant to conventional dose CHOP chemotherapy for patients with diffuse aggressive NHL in high-intermediate & high risk IPI

59909—A Phase II Study of Intensive Induction Chemotherapy Followed by Autologous Stem Cell Transplantation Plus Immunotherapy for Mantle Cell Lymphoma

79804—Issues of Survivorship among breast cancer Survivors

79806—Prostate cancer prevention using dietary soy supplements.

90006—A Phase II Study of Estramustine, Docetaxel, and Bevacizumab (anti-VEGF Antibody) in Men with Hormone Refractory Prostate Cancer

99808—Docetaxel/Est vs Mitox/Prednisone (SWOG 9916)

99813—Docetaxel/Estramustine/Carboplatin/GCSF for HRPC

309801—Determination of Utilities for Control of Chemotherapy-Induced Nausea or Vomiting

Thank you to organizations supporting CALGB in 2001

The following organizations have provided assistance to support CALGB research activities this year:

Agouron Pharmaceuticals

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Amgen, Inc.

Arrow International

Aventis Oncology

Breast Cancer Research Foundation

Bristol-Myers Squibb Oncology

Chiron Corporation

Gilead Sciences

GlaxoSmithKline

Genentech BioOncology

Immunex Corporation

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Ortho Biotech, Inc.

and the Janssen Research Foundation

Pharmacia Corporation

Roche Pharmaceuticals

Sanofi-Synthelabo

Schering Corporation

SmithKline Beecham

SuperGen Pharmaceutical Research Institute

T.J. Martell Foundation for Leukemia, Cancer
and AIDS Research

Wyeth-Ayerst Pharmaceuticals

CALGB CALENDAR

Fall 2001 Core Meeting*	September 6-9	Raleigh-Durham, NC— <i>Sheraton Imperial Hotel</i>
Fall 2001 GU Core Meeting*	September 13	Chicago, IL— <i>O'Hare Airport</i>
Fall 2001 GI Core Meeting*	September 21	Chicago, IL— <i>O'Hare Airport</i>
Fall 2001 Group Meeting	November 15-18	Jacksonville, FL— <i>Amelia Island Plantation</i>
Winter 2002 Core Meeting*	March 1-3	Chicago, IL— <i>Fairmont Hotel</i>
Summer 2002 Group Meeting	June 13-16	Washington DC— <i>Omni Shoreham Hotel</i>

**closed meetings open to cadre members of core committees and invited guests*

PROFESSIONAL MEETINGS

AACR

American Association for Cancer Research

Oct. 17-21, 2001

Palm Desert, CA

International Kidney Cancer Symposium

Kidney Cancer Association

Oct. 26-28, 2001

Chicago, IL

ASTRO

American Society for Therapeutic Radiology & Oncology

Nov. 4-7, 2001

San Francisco, CA

ASH

American Society of Hematology

Dec. 7-11, 2001

Orlando, FL



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