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Cancer Imaging: Moving Clinical Research Forward

Inside . . .

CALGB Cancer Imaging..... p. 1

Message From The Group Statistician p. 2

Oncology Nursing Perspective p. 3

Training Update p. 5

CALGB Publications 101 p. 6

CALGB Group News p. 8

Protocol News p. 9

CALGB Support p. 11

Imaging – X-ray, PET/CT, MRI, ultrasound, radiation therapy and other procedures – has rapidly become a dynamic change agent in the field of clinical oncology. Moving beyond screening, staging and following disease recurrence or progression, imaging offers a closer, more intimate biological view past tumors and organs to tissues, cells and molecules – all in a non-invasive way with up-to-the-minute detail. Cancer imaging provides information that helps practitioners determine which patients may fare better on certain regimens and whether they are responding to treatment.

The CALGB Imaging Committee, which formed in 2002, along with the Imaging Core Laboratory (ICL) at The Ohio State University, have been leveraging such developments, leading the charge in a cooperative group setting. Chaired by Lawrence Schwartz, M.D., Professor of Radiology and Chairman of the Department of Radiology at the Columbia University Medical Center, the committee aims to improve the use of imaging biomarkers as a method for therapeutic response assessment in CALGB trials. It also works to introduce newer imaging techniques into the trials and further develop its core facility (ICL) to assist in image data collection, quality control and

interpretation. Currently, the committee is collaborating with CALGB disease committees on more than 10 protocols by proposing specific imaging objectives and response assessment techniques to advance imaging science in oncology. These studies include: use of FDG-PET/CT for the early assessment of tumor response in patients with esophageal cancer, non-small cell lung cancer, Hodgkin lymphoma and non-Hodgkin lymphoma; use of contrast-enhanced dynamic MRI for tumor angiogenesis in breast and renal cell carcinoma; and a pilot study to examine micrometastases in the local nodes of the pelvis in patients with bladder carcinoma

— see **CALGB IMAGING COMMITTEE**, page 10

Cancer and Leukemia Group B

Central Office
230 W. Monroe Street
Suite 2050
Chicago, IL 60606-4703
(773) 702-9171
www.calgb.org

MESSAGE FROM THE GROUP STATISTICIAN

Our Main Mission:

Advancing the Science of Cancer Research



Daniel J. Sargent Ph.D.

It is my great pleasure to write this first column in my new role as the CALGB Group Statistician. The shoes I have the honor to fill, those of Dr. Stephen George, are large indeed. Dr. George's contributions to the CALGB are immeasurable, permeating every fiber of the CALGB. He has assembled, mentored and nurtured an innovative, talented and dedicated staff at the CALGB

Statistical Center whose work with the CALGB will continue for years to come. On behalf of myself, and the entire CALGB Statistical Center, thank you Steve.

I am commonly asked: "Why did you want the CALGB Group Statistician position?" My response is simple: The CALGB is the premier cancer research organization in the country, and has the greatest ability to do what really matters – help cancer patients. All of the scientific, administrative, organizational, technical and statistical expertise within the CALGB Statistical Center is dedicated to this goal, and in this regard, the scientific resources of the CALGB are without equal.

To pursue this goal, every statistical center should have one primary mission: to advance the science of cancer research. This mission is accomplished by three primary aims:

1. Hire, train and retain dedicated faculty statisticians with a passion and skill for innovation in statistical, translational and clinical research.
2. Deeply integrate the statistical center staff (faculty and staff statisticians, and data management and IT staff) into the ongoing research activities of the Group.
3. Develop and continually improve efficient IT and human systems and processes to maximize efficiency and timeliness.

The CALGB Statistical Center at Duke has a record of excellent performance. A key strength is the statistical faculty, who are engaged, motivated and dedicated to the research of the CALGB. Important advances have been made within the Statistical Center, including in the expanding field of bioinformatics. The data management unit is well coordinated and efficient, and the IT unit has developed multiple tools and systems that streamline critical group functions. Within the CALGB, we now have a remarkable opportunity, through a partnership with existing resources at my home institution

(the Mayo Clinic), to rapidly advance the CALGB agenda through enhancements to these existing systems.

The rapid implementation of an electronic data environment to the CALGB for capture, management and quality control is of highest priority. This is critical not only for increased efficiency but also for good science – we must have accurate, reliable data available in real-time to allow rapid trial assessment and possible modification. The CALGB is in a highly advantageous position to take advantage of a massive institutional commitment the Mayo Clinic has made toward implementing a state-of-the-art data collection and management system, Medi-data RAVE. By mid-2011, all new CALGB trials will be launched in RAVE, and transitions of ongoing studies into RAVE will be initiated. The RAVE package will be used for multiple functions beyond data capture, including forms tracking, delinquency monitoring, query management, quality review and clinical end-point verification. RAVE streamlines data management in the cooperative group setting, allowing us to better use our existing resources. By placing heavy emphasis on standardized data elements and a comprehensive set of point-of-entry checks, the data quality control requirements post-entry are significantly reduced and standardized.

When data is collected and processed in a highly standardized manner, efforts of the statisticians can be focused on the area of greatest need – scientific collaboration and leadership. In this regard, the short- and long-term plan for the statistical function within the CALGB is to recruit and involve the most talented statistical faculty possible, which in this case will be realized by retaining the existing faculty at Duke. To increase the ability of faculty statisticians to focus on science, a third level of statistical staff for the CALGB will be introduced. This position, that of a statistical programmer analyst at a bachelor's level, is a position that has been highly successful at the Mayo Clinic.

In this limited space, I can only provide a brief description of a few exciting innovations that the statistical center will bring to the CALGB over the coming months and years. Future columns will include further details. At all times, I am eager to hear (and mostly importantly, to learn) from CALGB members about issues, challenges and progress to date. Thank you all for your enthusiastic welcoming of me into this role, and particularly to the CALGB Group Chair, Dr. Bertagnolli, for her confidence and support. I genuinely look forward to working with you for years to come.

Workload Assessment in Clinical Trials

By Denise Friesema, M.S., R.N., O.C.N.
University of Chicago Medical Center

The clinical trial landscape is becoming increasingly complex with rapid changes as a result of mounting regulatory requirements and escalating costs.¹ As a result, lack of sufficient support for the necessary infrastructure to carry out the clinical trial work with high quality and efficiency has become a critical problem.² Workload in clinical trials continues to escalate without incremental staffing as a result of an increasingly stringent regulatory environment, the economics of doing more with less and emphasis on funding and productivity. As new protocols are developed, they are becoming more complex due to combined multimodality therapies and the evolution of personalized cancer care.³

Over the past 10 years in drug development, new and innovative therapies (such as tissue evaluation for mutations like KRAS) have emerged, resulting in additional work. Despite the increase in complexity of the clinical trial, staffing models have not changed. A focused assessment of a clinical trial is necessary to provide benefits such as improved efficiency, management and budgeting. As well, measurement of workload allows for professional development through definitions of professional standards for workload, education, training, certification and salary. Furthermore, workload assessment allows for role delineation and alignment of a proper staff mix.

Current methods of workload assessment focus on the numbers of clinical trials, monitoring visits per month and subjects on a clinical trial.⁴ These methods result in



research coordinator burnout, crisis management and staff retention challenges.⁵ There are inherent barriers in measuring clinical trial workload. Clinical trial tasks are complex, unpredictable, varying and are not entirely within the realm of the research coordinator's control. In addition, diversity in the clinical trial setting, roles and responsibilities of the coordinator, along with education and training, pose additional challenges. Poorly defined workload measures exist at present and further clarity is needed regarding what to measure, the scope of the measurement and the credibility or reliability of such measures.

Literature Review

A review of the literature suggests that clinical research infrastructure, and in particular, workload assessment is little noted and rarely studied.¹ There appears to be no consensus on a model for evaluating workload in the clinical research infrastructure. Furthermore, no clear guidance has been published on what the maximum workload is in terms of research coordinator-to-subject or coordinator-to-protocol ratios. Current literature focuses on utilization of accrual data, acuity or a points scale and task and time necessary in a clinical trial. Utilization of accrual data is the most basic and rudimentary measure of workload. Such measure focuses on the numbers of studies and subjects compared to the number of staff available to do the work. Use of just accrual data does not account for screen failures, subject dropouts or the time necessary to complete each task.

A points system was first published in 1992 by the Cancer Clinical Investigations Review Committee (CCIRC) as a means for cooperative groups to determine budget allotments.⁸ Credits were assigned based on the phase or type of study, follow-up requirements and/or subjects enrolled at affiliates. The

— see **ONCOLOGY NURSING**, next page

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ONCOLOGY NURSING PERSPECTIVE

continued from page 3

algorithm identified that one full-time employee (FTE) could adequately manage 40-50 credits inclusive of new accruals and subjects in follow-up.⁸ Meant to determine finances of the clinical trial, the CCIRC algorithm was inappropriately adopted by sites to assess productivity and make day-to-day staffing decisions.

In 2000, Gwede published the results of a self-reported workload study of coordinators affiliated with the Radiation Therapy Oncology Group (RTOG). Two hundred and sixty-five coordinators were surveyed with 107 responding, a 40.4 percent response rate.^{7,9} Gwede's study evaluated the time it took to complete tasks compared to the number of patients in the trial. Gwede noted that workload assessment tools that acknowledge the intensity of the work and the effort spent are essential to establishing standards and facilitating growth of the clinical research coordinator profession.^{7,8} Gwede provided no clear recommendation on a formula but identified an urgent need for practical and meaningful workload assessment tools.^{7,8}

Another study evaluating the workload of cancer clinical trials was published by the National Cancer Institute of Canada (NCIC) in 2002. Roche et al focused on task-oriented time measures and, in general, confirmed that workload varies by task, phase of study, sponsor type and stage of protocol. NCIC identified that documentation and handling of special procedures were the most time-consuming tasks.¹⁰ The NCIC also identified that industry studies were more labor-intensive than studies with other sponsors. NCIC also published that phase I, I/II and II trials were more intensive when compared to phase III trials. Unfortunately, this publication made no recommendation of a standardized tool to assess workload.

In a publication in 2003, Fowler and Thomas focused on a more quantitative approach by assigning an acuity score to a protocol. Such a system seeks to evaluate the degree of difficulty and resource necessary for a given study establishing a sound basis for assigning coordinator support and predicting staffing needs. In their work, Fowler and Thomas established a tool whereby a protocol is scored numerically to allow for comparison across the clinical trials of a particular coordinator or site. Study-required procedures and data collection time points were identified and tabulated for the first year of each study.⁶ The approximate time necessary to complete the task was also determined.⁶

Such measures allowed calculation of the time it would take to complete all tasks required by the coordinator for one subject through one year of participation.⁶ A pilot review of two trials presumed to be of equal workload was completed and revealed that study one required 8.5 hours per patient of coordinator time versus 29.5 hours for study two.⁶ Further evaluation of all studies determined that each coordinator had a workload that ranged from 500-750 points per coordinator.⁶ During subsequent review and discussions, it was determined that an appropriate intensity was between 500-650 points.⁶ Fowler and Thomas noted that additional research should be conducted as a means to explore site management tools such as acuity scoring. In 2005, Devine et al published a paper focused on coordinator time and effort in the Children's Oncology Group (COG). Devine et al, concluded that focusing on tasks rather than accrual was a correct approach but, again, no definitive recommendation was made regarding a tool.⁵ Berridge and Coffey published a similar work in 2008 evaluating time spent on activities through the European Organization for Research and Treatment of Cancer (EORTC). Supporting the work done by Roche et al, in 2002, Berridge and Coffey identified all the main tasks and subtasks involved in a clinical trial as a means to quantify workload.³

The Clinical Trials Working Group (CTWG) Operation Efficiency Initiative launched by the National Cancer Institute made public a "working document" in 2009 entitled NCI Trial Complexity Elements and Scoring Model. The model recommends aligning reimbursement for NCI-sponsored trials with trial complexity as one element for an improved funding paradigm.¹¹ Ten elements were selected for the model representing the most complex and time-consuming details of a trial management. The 10 trial elements were: number of study arms, informed consent process, registration or randomization steps, complexity of investigational treatment, length of investigational treatment, feasibility and personnel impact, data collection complexity, follow-up requirements, ancillary studies and participant feasibility and enrollment.¹¹ Each element was subdivided into three categories for rating as either standard, moderate or high. The categories were then provided a numerical scoring that included zero points for a standard complexity, one point for moderate and two points for high complexity.¹¹ Like the model published in 1992 by the Cancer Clinical Investigations Review Committee, this complexity scoring model also seeks to align trial complexity with funding. However, considering the elements identified,

— see **ONCOLOGY NURSING**, page 8

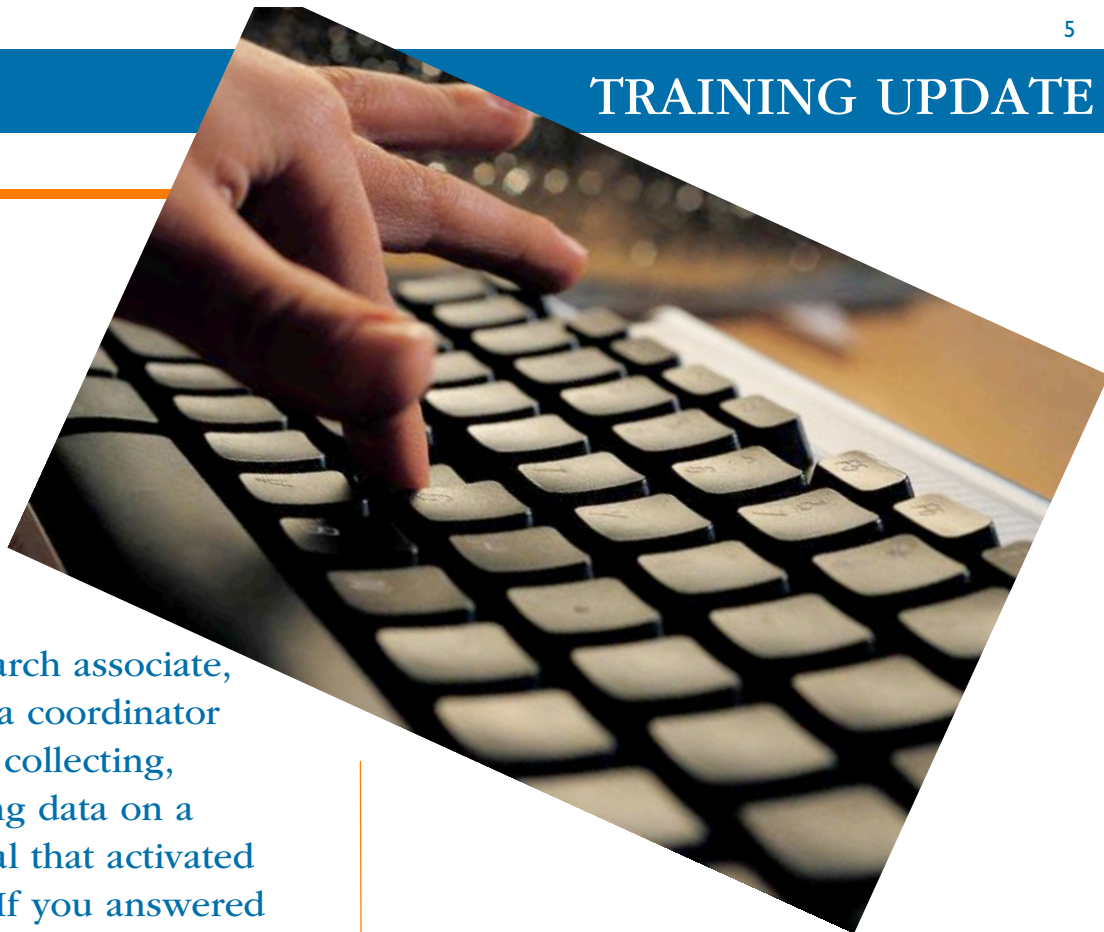
New Online RECIST 1.1 Training Now Available

Are you a clinical research associate, oncology nurse, or data coordinator who is responsible for collecting, reporting, or monitoring data on a CALGB solid tumor trial that activated after November 2009? If you answered *yes* – or if you are curious about the changes in the Response Evaluation Criteria in Solid Tumors (RECIST) – then this 20-minute online training module is for *you*.

What You Will Learn

CALGB Statistical Center Clinical Trials Manager Susan Barry provides a brief overview of the original RECIST 1.0 criteria and then summarizes what has not changed in the new criteria. From there you will learn changes that affect how you measure target tumor burden; which lesions are considered non-target lesions; how to assess lymph nodes and bone and cystic lesions; the new definitions for response and progression; what to do when lesions become too small to measure, split, coalesce, or reappear; and much more.

Through a series of examples, you will see how the same set of measurements can yield different results when evaluated using RECIST 1.0 versus RECIST 1.1. Finally, you will learn how CALGB has implemented the updated criteria and you'll get a walk-through of the C-2000, a new solid tumor evaluation form for all CALGB trials using RECIST 1.1.



How to Access the Training

For your convenience, this module is available on-demand on the CALGB Member Web site under the Training tab. Just look for the RECIST 1.1 link under Disease Response. To access the module directly, type <https://training.calgb.org/recist1p1> in the address bar in any Internet browser.

Don't Forget to Send Us Your Feedback

We want to hear what you think of the training we create for you. Send your comments, suggestions or questions to CALGBTraining@mc.duke.edu.

CALGB PUBLICATIONS 101

HELPFUL TIPS & TIDBITS

PART I – FLOW OF INFORMATION ON CALGB CLINICAL TRIALS AND RESULTS

For CALGB investigators, publishing the results of CALGB trials is the final and most important step in the research path. The preferred end result is a manuscript published in one of the major peer-reviewed oncology journals, presenting the final results of the clinical trial with a thorough analysis and discussion of its significance. That process can take from months to years after a study completes accrual, depending on the study objectives and end points. In the meantime, there are several other documents produced by the CALGB that provide information, if not results, about ongoing and recently closed trials. Here's a quick list of these documents that describe a clinical trial throughout its course, from the first proposal to the final results manuscript.

Clinical Trial Protocol

This document describes the study in full. It details what will be tested and states the rationale behind the study design as well as the study objectives. Other major elements are eligibility criteria, data submission requirements and, for treatment trials, treatment schemas and detailed treatment guidelines. Also included are model consent forms—documents that explain the trial in terms typical patients can understand so that they can be truly informed about the risks of the trial before they consent to participate.

Protocol documents contain privileged and confidential information not for distribution to the general public. The primary concerns are for patient safety and to ensure that the experimental treatment regimen is not used on an ad hoc basis off-study by non-affiliated oncologists. Protocol documents are distributed to CALGB institution and other participating cooperative groups' institutions through the CALGB Member Web site.

Brochures for Patient Education and Physician Reference

Occasionally, extra brochures will be prepared to inform patients and health care providers about a clinical trial in which they may be able to participate. Any literature given to patients explaining or urging participation in a trial must first be approved by the hospital's Institutional Review Board (IRB). CALGB study chairs interested in using educational literature are encouraged to work with CALGB Central Office to ensure that the information is conveyed appropriately.

Agenda Book Statistical Summaries

Every year, CALGB publishes statistical summaries of its open clinical trials and makes them available on the CALGB Member Web site prior to its annual Group meeting. The reports summarize the major aspects of the trial from the original protocol document, and include study objectives, schematic design of the study, eligibility requirements, and data submission requirements. They are updated every year to incorporate any changes or amendments to the study, and include the most recent accrual and toxicity data. No study results are reported in these summaries, as these studies are still open and ongoing.

Statistical summaries are also confidential documents, not for general public distribution. Accrual and toxicity information in these study summaries can be shared with parties who have a medical or regulatory interest, but the information cannot be published without permission of the Group chair.

Published Abstracts

Often the first publicly available information about a study's results is published as a brief summary for the annual meetings of major oncology organizations. The two largest publishers of abstracts on cancer clinical trials are *Blood* (the journal of the American Society of Hematology), and ASCO (the American Society of Clinical Oncology). ASCO also publishes the *Journal of Clinical Oncology*. These abstract reports are very brief (300 words or less); however, they are not always the final or complete results.

Manuscripts

The CALGB considers a study's results to be officially *published* once a manuscript reporting the primary study results has been printed in a peer-reviewed medical journal. Manuscripts reporting results of CALGB trials can be submitted to journals for consideration only after review by the CALGB Central Office, Statistical Center, and a Group review by the principal investigators at all the CALGB main or at-large member institutions. This is considered the CALGB Group Review. Please see the manuscript publishing guidelines on the next page for more information.

— more **CALGB PUBLICATIONS 101**, next page



MORE HELPFUL TIPS & TIDBITS

PART II – HOW TO PUBLISH A CALGB MANUSCRIPT

The following steps are taken from the CALGB Policies and Procedures Manual – Section 10: Publications, which can be found on the CALGB Member Web site under Policies. They are intended to serve as a reference aid for study chairs and committee chairs.

First Up: CALGB Statisticians

After a study closes, and all the final patient data forms are submitted (for phase III studies: after the Data and Safety Monitoring Board, or DSMB, determines that the study results can be released), the study statistician meets with the study chair to discuss study results and what analyses will be needed. The statistician has to approve reporting of any results from a CALGB study, whether for an abstract or a manuscript.

Writing Assistance

Guidelines for preparation of research manuscripts are available online from many of the major oncology journals. A good resource can be found on the Information for Contributors page on the *Journal of Clinical Oncology* Web site at <http://jco.ascopubs.org/site/ifc/prepguide.xhtml>.

Manuscript Structure

A typical manuscript reporting the results of a clinical trial is organized according to a standard structure. Much of the material can be derived from the protocol document. The Introduction and Methods sections are usually derived directly from the protocol. The Results section will be prepared by the statistician in the final analysis report. Most of the references are already in the protocol document. New writing is needed primarily for Abstract and Discussion sections.

Co-authorship Rules

Determining co-authorship on manuscripts is often the most complicated aspect of the publishing process. The CALGB policy is to give co-authorship credit based on workload and intellectual contributions, as well as for efforts in recruiting and enrolling patients to the study (accrual). The study chair (primary author) and the committee chair (who is usually the last listed co-author) have final responsibility for naming all the other co-authors.

Order of names. Listed after the primary authors are the faculty statistician and/or staff statistician, followed by

other major collaborators and contributors. Institutional co-authors named for accrual should be listed next, with the final author positions reserved for the committee leadership.

Criteria for institutional authorship. Study accrual tables are used to determine which institutions (or networks) will be awarded institutional co-authorship. The number of patients needed varies according to the total number of patients in the study. *Refer to the CALGB Policies and Procedures Manual or contact the publications coordinator (pubscoord@calgb.org) for accrual thresholds.* The principal investigator at each eligible institution will name the researcher from his or her institution or network to receive the co-authorship.

Intergroup studies. For intergroup studies, co-authorship is given to at least one representative from every participating group – usually the cooperative group's study chair. Authorship should also be awarded to statisticians and discipline coordinators with significant intellectual or workload contribution, as well as to investigators with high accrual per the institutional coauthorship criteria above. The committee chairs and study chairs from the participating cooperative groups should establish authorship guidelines for the intergroup study before study activation.

Title Page and Credits

- The title of every manuscript should state that this is a Cancer and Leukemia Group B (CALGB) study, and include the CALGB protocol number.
- Co-authors should be listed at the institution where they did the primary work on the study. For each co-author, the institution name, city and the author's NIH grant number should be listed in the footnote.
- The Central Office provides an additional appendix acknowledging all the CALGB institutions that accrued patients to the study (CALGB main and at-large members and CCOP networks). This includes the institution location, principal investigator's name, and NIH grant number.
- In the case of intergroup studies, the acknowledgements will list the participating CALGB institutions, but only the headquarters offices and chairs of the other participating cooperative groups.
- Special acknowledgements should be given when industry partners, foundations or other organizations that have supported aspects of the study. (*This funding may also require the study chair to submit a final draft*)

CALGB GROUP NEWS

STAFF UPDATES

@ The Central Office

Shivani Shah joins the CALGB as a Protocol Coordinator assigned to the CALGB GI Committee. She brings experience from her positions as a Research Assistant at the University of Illinois at Urbana-Champaign, a Pharmacy Service Representative at Caremark, and a Training Operations Coordinator at Children's Memorial Hospital.

Morgen Alexander-Young, M.P.H., also comes to the CALGB as a Protocol Coordinator. She is assigned to the CALGB Lymphoma Committee. Recently, she worked as a Project Coordinator at the University of Chicago and has had experience as a Research Assistant.

Bernice Williams joins the CALGB as an Executive Assistant. She has worked as the Hematology/Oncology Fellowship Program Coordinator at the University of Chicago and was also a Special Assistant at the university's Pritzker School of Medicine.

Benjamin Kleinman, formerly a CALGB Senior IT Analyst, has transitioned to Project Manager in CALGB Protocol Operations. He is now responsible for monitoring the progress of study development, ensuring adherence to timelines and identifying and analyzing issues that impact study development.

Oncology Nursing Perspective

continued from page 4



the model should be explored for applicability to workload assessment.

Implications

In summary, no publications to date provide a definitive formula or tool for workload assessment. A majority of the work has focused on NCI-funded clinical trials and workload assessment. Such models have been fixed on complexity for purposes of financial modeling and not necessarily staff workload and allocation of the work. The publication by Fowler and Thomas is the only one describing a complexity scoring applicable to industry sponsored clinical trials. The publications are lean but suggest that measurement of workload using an evaluation of time and task appears to be the best approach. Nonetheless, more questions than answers are generated and further exploration of other variables including screen failures, queries, long-term follow-up, phone calls and re-consenting, to highlight a few, are essential as components of workload measurement. Further research is needed to evaluate published models for reliability, validity

and exploration of applicability to industry sponsored and investigator initiated clinical trials. Research on the impact of workload on a coordinator and factors associated with staff burnout also need to be better understood.

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BREAST COMMITTEE**OPENED**

CTSU—NCIC: MA.32: A phase III randomized trial of the effect of metformin versus placebo on recurrence and survival in early stage breast cancer

Study Chair: J. Ligibel

CLOSED

40101—Cyclophosphamide and doxorubicin (CA X 4 cycles) versus paclitaxel (4 cycles) as adjuvant therapy for breast cancer in women with 0-3 positive axillary lymph nodes: A phase III randomized study

Study Chair: L. Shulman

CCHO COMMITTEE**CLOSED**

70301—Quality of life, employment and informal care cost analysis in women receiving adjuvant chemotherapy for breast cancer with 0-3 positive axillary lymph nodes

Study Chair: B. Hillner

GU COMMITTEE**OPENED**

90802— Randomized phase III trial comparing everolimus plus placebo versus everolimus plus bevacizumab for advanced renal cell carcinoma progressing after treatment with tyrosine kinase inhibitors

Study Chair: G. Philips

LEUKEMIA COMMITTEE**CLOSED**

10503—Phase II study of maintenance therapy with decitabine (NSC #127716, IND #50733) following standard induction and cytogenetic risk-adapted intensification in previously untreated patients with AML < 60 years

Study Chair: W. Blum

CALGB Publications 101

continued from page 7

of the manuscript to the funding organization before publication – authors will be contacted by the CALGB in such cases.)

Review Process

Co-authors' Review. Once the initial draft is complete, the study chair sends it to all the listed co-authors for review *before* submitting it to the CALGB Central Office for Group Review.

CALGB Group Review. The study chair sends a revised draft to the CALGB Central Office for Group Review (pubscoord@calgb.org). After processing, the publications coordinator distributes copies to manuscript reviewers at the Central Office, the CALGB Statistical Center, and to the principal investigators at all CALGB main and at-large member institutions and CCOP networks.

Reviewers are given 30 days to respond with comments directly to the study chair. (*Faster review cycles are permitted; requests stating the reason for expedited review are sent to the Group chair for approval.*) After the review period has lapsed, the study chair can then make final changes and submit the manuscript directly to the desired medical journal.

Notification. Study chairs must keep the publications coordinator apprised of the status of all manuscripts submitted to medical journals. Copies of letters of acceptance and the final printed article should be sent to the Central Office (pubscoord@calgb.org).

Timeline

The publication process starts when the DSMB releases the study data or final patient data forms are received. After consultations with the study chair, the faculty statistician prepares the statistical analysis and a final report. Once those are completed, the clock starts ticking: the expected time range is as follows:

- First draft of manuscript ready for co-author review: *3-6 months*
- Co-author review: *1 month*
- Revisions based on co-author feedback; revised draft ready for Group Review: *1 month*
- Group Review: *1 month*
- Final revisions based on Group Review feedback; final draft ready for journal submission: *0-1 month*

Total time from completion of statistical analyses to manuscript submission: *6-10 months.*

The study chair, committee chair and faculty statistician should establish a publication schedule and deadlines at the start of the publication cycle. It is critical that the study chair communicate regularly with the committee chair about publication progress. If the study chair is unable to complete the manuscript in a timely fashion, the committee chair may delegate writing responsibility to the next best-qualified author. Study chairs who are unable to complete manuscripts run the risk of being excluded from chairing future CALGB studies.

CALGB IMAGING COMMITTEE

continued from page 1

with MRI. As another example, CALGB 580601 (an embedded companion to CALGB 80302—A phase II trial of preoperative irinotecan, cisplatin and radiation in esophageal cancer) is part of a trial in which PET imaging is a key correlative endpoint to determine if PET imaging can be used to predict response or progression of disease at the induction therapy time point.

Another companion study, CALGB 580602 (part of CALGB 140503—A phase III randomized trial of lobectomy versus sublobar resection for small (≤ 2 cm) peripheral non-small cell lung cancer), will systematically analyze primary tumor characteristics and nodal disease seen by PET and standard contrasted enhanced CT in a trial of wedge resection versus lobectomy of small stage IA NSCLC. Wedge section is an attractive alternative to traditional lobectomy in patients with compromised pulmonary function if there are indeed comparable DFS and survival rates. Image analyses will include PET and CT characteristics of primary tumor, determining the false-negative rates of involved hilar and mediastinal nodes, and assessing the usage of annual follow-up CT after surgical resection.

Two cooperative studies (CALGB 150007—Contrast-enhanced breast MRI, MRS and correlative science studies to characterize tumor response in patients undergoing neoadjuvant treatment for locally advanced breast cancer and CALGB 150012/ACRIN-6657—Contrast-enhanced breast MRI and MRS for evaluation of patients undergoing neoadjuvant treatment for locally advanced breast cancer) systematically examine the utility of the patterns and intensity of contrast enhancement of breast lesions in patients receiving neoadjuvant therapy for stage III breast cancer. A subgroup of patients will also undergo MRS focusing on the changes in choline with therapy, correlated with other molecular markers and treatment response. Thirty patients will also undergo two serial MRS exams prior to chemotherapy to address the test/re-test variability of MRS. Image analyses are being performed collaboratively with the American College of Radiology Imaging Network (ACRIN).

The Imaging Committee is also developing protocols to address using imaging in managing patient therapy. Two such protocols were recently opened: CALGB 50604—Phase II trial of response-adapted chemotherapy based on positron emission tomography for non-bulky stage I and II Hodgkin lymphoma, and CALGB 50801—Phase II trial of response-adapted therapy based on positron emission tomography (PET) for bulky stage I and stage II classical Hodgkin lymphoma (HL).

These are among the first in the country to systematically use early PET/CT results to guide therapy and it is hoped, decrease treatment morbidity without adversely effecting survival in patients with non-bulky and bulky stage I and II Hodgkin disease.

Another imaging protocol that opened earlier this year is CALGB 80802—Phase III randomized study of sorafenib plus doxorubicin versus sorafenib in patients with advanced hepatocellular carcinoma (HCC). It will use quantitative perfusion methods and correlate with outcomes outcome in patients with advanced HCC randomized to sorafenib only or sorafenib and doxorubicin treatment groups. It is hoped that these quantitative technique will be a better surrogate marker in liver tumors with poorly defined tumor margins and treatment response in tumors that do not change in size, but undergo extensive central necrosis.

On a broader level, the committee is collaborating with ACRIN and the Quality Assurance Review Center (QARC) on the VIEW Consortium that will provide CALGB Imaging Core Laboratory services to the NCI-sponsored cooperative, and possibly, other NCI-sponsored clinical trial programs. The consortium's main goals are to develop an inter-operative IT infrastructure across the network to collect, distribute and archive images obtained on NCI-sponsored trials that use VIEW; develop standard operating procedures for acquiring and assessing imaging endpoints in cancer clinical trials and an approach to standardizing newer imaging markers; and develop a standardized approach to credentialing facilities that perform imaging exams according to VIEW standards.

What's Next?

The Imaging Committee plans to continue its efforts to recruit members who are willing to participate in cooperative group trials and lend support in the development of the imaging portions of the trials. It also plans to further develop bidirectional interactions with CALGB disease committees and encourage the use of Imaging Committee expertise in the design and interpretation of clinical trials.

CALGB Imaging Committee & Core Lab

Committee Chair: Lawrence Schwartz, M.D., Professor of Radiology and Chairman, Department of Radiology, Columbia University Medical Center

Vice Chair: Nathan Hall, M.D., Ph.D., Assistant Professor of Radiology, The Ohio State University

Core Lab Director: Michael Knopp, M.D., Ph.D.

Core Lab Project Manager: Jun Zhang, Ph.D.

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

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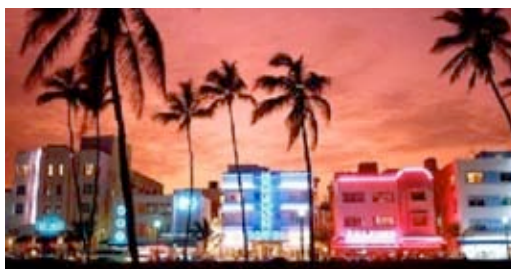
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2010-11 Cancer and Leukemia Group B Meetings



Fall Group Meeting
November 11-13, 2010
The InterContinental Miami
Miami, FL



Spring Committee Meeting*
March 3-5, 2011
Westin O'Hare
Chicago, IL

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



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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.

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Mary A. Sherrell, M.A., Treasurer, CALGB Foundation, 230 W. Monroe Street, Suite 2050, Chicago IL 60606
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