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Wanted: Methods To Measure Or Estimate Renal Function For Dosing Cancer Drugs

By Paul Goldberg

NCI and FDA are confronting a daunting problem: finding an evidence-based method for dosing carboplatin and many other drugs that are dosed based on renal function.

Though the carboplatin controversy first became widely known earlier this month, it started simmering at least 21 years ago, playing out in medical literature.

"Everyone has been using their own approach for assessment of renal function," said Judith Smith, associate professor and director of pharmacology research at the MD Anderson Cancer Center's Department of Gynecologic Oncology and Reproductive Medicine. "Whatever position you want to

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In the Cancer Centers:

Hutchinson Center Receives $14 Million NCI Grant For Immunotherapy Trials Network

FRED HUTCHINSON CANCER RESEARCH CENTER member **Martin Cheever** received a U01 grant from NCI to fund the Cancer Immunotherapy Trials Network, with approximately $14 million budgeted for total costs over five years.

The CITN will support a multi-investigator team that will be assembled to bring new immunotherapy agents to the clinic. The emphasis will be on clinical trials of "high priority" agents that were identified at the 2007 NCI immunotherapy agent workshop and on clinical trials using combinations of immunotherapy modalities and other agents. Trials will incorporate high quality, centralized immuno-monitoring services, along with biomarker assessment and correlative studies using patient samples. Up to 25 institutions will conduct the clinical trials as CITN member sites. The NCI will provide data coordinating services for the CITN using other funds.

UNIVERSITY OF MICHIGAN researchers received a $9.4 million award by the NIH-FDA Joint Leadership Council to spearhead collaborative activities to stimulate a new research in regulatory science. The three-year project, "Accelerating Drug and Device Evaluation through Innovative Clinical Trial Design," is led by **William Barsan**, chair and director of the U-M Department of Emergency Medicine; **Donald Berry**, senior statistical scientist and founder of Berry Consultants, and **Roger Lewis**, co-chair of

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Dosing Problem In Oncology Extends Beyond Carboplatin

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take, you are likely to find something in the literature to support your position."

The problem with dosing the drug that is widely used in the treatment of lung and gynecological cancers became widely known on Oct. 1, when the NCI Cancer Therapy Evaluation Program issued an "action letter" instructing principal investigators of government-sponsored trials to amend the protocols by capping the doses of carboplatin (The Cancer Letter, Oct. 8).

NCI officials say they are planning to study the dosing problem in prospective trials. Since the problem is likely fundamental, in a matter of days, the institute will send out another letter, offering further explanation of the problem, sources said.

A week after the CTEP letter, FDA sent a bulletin notifying members of the American Society of Clinical Oncology about questions raised on dosing carboplatin. The problem became urgent because a standardized test for measuring serum creatinine—the Isotope Dilution Mass Spectrometry assay—produces lower values than tests previously used in calculation of the patients' doses.

"If the total carboplatin dose is calculated based on IDMS-measured serum creatinine…, carboplatin dosing could be higher than desired and could result in increased drug-related toxicity," the agency said in the letter to ASCO members.

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Other insiders point out that in some cases, depending on the formulas and other criteria used, the dose can also be lower.

The dosing question affects 98 ongoing NCI-sponsored trials and as many as 175 industry-sponsored trials that use carboplatin. There is also the question of dosing methods used off-protocol.

No one knows how well rank-and-file oncologists understand the controversy and whether they even know that the assays have changed. How the drug is given in the context of standard care is anyone's guess. Toxicities observed would be unlikely to strike an average oncologist as out of the ordinary and it's unlikely that they would be reported to adverse events monitoring systems.

Carboplatin is the only drug dosed exclusively based on renal function. However, the doses of a wide range of oncology drugs—and a lot of drugs outside oncology—are initiated or adjusted based on renal function. These include bleomycin, capecitabine, cisplatin, methotrexate, pemetrexed, fludarabine, lenalidomide, high dose cytarabine, high dose melphalan, pentostatin, topotecan, zoledronic acid, and pamidronate.

"We feel very strongly that we as a community must perform new clinical trials to determine the optimal way to dose carboplatin and, indeed, other renally cleared oncology therapeutics," said S. Percy Ivy, associate senior investigator at NCI's CTEP.

No one is objecting to the NCI's efforts to launch prospective studies to find the optimal way to give carboplatin. However, the stopgap measures proposed by the institute and communicated to oncologists by FDA are more controversial.

Letters from CTEP and FDA instruct doctors to cap the dose of carboplatin at 125 mL/min. According to the FDA letter, the IDMS method appears to underestimate serum creatinine values compared to older methods when the serum creatinine values are relatively low (e.g., ~0.7 mg/dL). A letter from the Gynecologic Oncology Group, a cooperative group, instructs investigators have to assign a creatinine level of no less than 0.6 mg/dL when they calculate the dose.

These safety measures run counter to some of the adjustments doctors and clinical pharmacologists have made over the years to deal with the uncertainty over dosing carboplatin.

Some have started using an adjustment for weight for patients who are obese.

"So far, everyone has been worried about toxicity, but some of us are equally worried about another

problem, underdosing," said Donald Harvey, director of the phase I clinical trials program at the Winship Cancer Institute of Emory University and president-elect of the Hematology/Oncology Pharmacy Association. "Dose capping suggested by NCI could lead to underdosing obese patients, depending on the calculations used to determine the dose."

Underdosing is hard to study.

"When we undertreat a patient, we don't know it, " Harvey said. "We simply see a treatment failure, which can be due to a variety of things, whereas when we overdose, we the side effects and we know that they are due to the drugs."

Much of the variability in calculation of the carboplatin dose occurs when doctors use the result of a serum creatinine test to estimate glomerular filtration rate, which is then plugged into the "Calvert formula" that cranks out the dose.

The letters from NCI and FDA state that it's possible to bypass the GFR estimation step by actually measuring the patient's GFR.

This is onerous and problematic on many levels, Harvey said. "This requires a nuclear medicine scan, increasing expense, time, and effort," he said. "Many clinicians will interpret the word 'measure' to mean a 24-hour urine collection. If this is really what's expected, I can see clinicians moving away from carboplatin."

The 24-hour urine collection requires the patient to collect and refrigerate every drop of urine over 24 hours. This was not what the British researcher Hilary Calvert did when he derived the formula for dosing carboplatin based on renal function. Calvert measured GFR using ^{51}Cr-EDTA, an isotope not available in the US.

There is no correlation between 24-hour urine collection and Calvert's measurement of GFR. "These estimates are all over the board," Harvey said. "There is a ton of variability out there."

Measurement of GFR is a serious problem, Ivy concurred. "We will be working closely with our clinical colleagues, pharmacologists, the FDA and the National Institute of Diabetes and Digestive and Kidney Disease to develop better validated methods for estimating GFR," she said.

Reliance on serum creatinine tests to estimate GFR is problematic, too. In fact, that was precisely what touched off the current controversy. Old serum creatinine tests, differed from each other and produced a range of values. The formulas for estimation of GFR differ as well.

MD Anderson's Smith has been grappling with variability in carboplatin dosing throughout her career. At first, she was interested in carboplatin hypersensitivity reactions. Later, her interest moved to dosing.

In 2002, she convinced the cancer center's gynecologic oncologists to adjust the doses for weight in obese patients.

"That was one of my first initiatives as a clinical pharmacist on the service that you need to account for obesity," Smith said. "You can't use their actual body weight. That's very well established in the literature. Ideal body weight underestimates it. Actual body weight overestimates it."

Like everything else in this saga, adjustment for obesity is controversial. Smith's preferred formula for converting serum creatinine into GFR—the Cockcroft-Gault equation—was first tested with the patient's actual body weight. The formula was derived primarily from a cohort of men and had to be adjusted for women. There were no obese patients in that population.

GOG has been using another formula for estimation of GFR based on serum creatinine—the Jelliffe formula. That equation doesn't account for weight.

In 2006, Smith started to collect data on patients receiving carboplatin at MD Anderson. The retrospective chart review has followed 399 patients. "We look retrospectively to see how doses were calculated vs. toxicities that occurred," Smith said. "And we compare using actual weight, adjusted body weight and ideal body weight."

Smith said she expects to complete analysis of the data by the end of the month. However, based on a snapshot analysis, she sent the following recommendations to CTEP:

• Establish Cockcroft-Gault as the equation that will be used to estimate creatinine clearance for assessment of renal function for dosing chemotherapy (narrow therapeutic agents). This has been done by GOG, a bastion of reliance on the Jelliffe formula, which doesn't adjust for weight, has abandoned that calculation method.

• Convert the reported IDMS SrCr value to the Non-IDMS SrCr based on equation released in initial letter on June 12th 2008 from Ortho Clinical Diagnostics [Non-IDMS SrCr = IDMS SrCr *1.065 + 0.067],

• When patient is obese (> 30% IBW), the adjusted body weight should be used in the CG equation; and

• Use an assigned SrCr of 0.8 mg/dL should be minimum threshold for estimating renal function.

"I applaud the NCI effort to study this," Smith said. "I am just saying that we can't wait that long to give people guidance in practice today. The studies will definitely help us refine and improve practice a year

from now, maybe two years from now, but the CTEP letter still leaves everyone in the conundrum of what weight do I use? What serum creatinine do I use? Do I adjust it to non-IDMS? There is such confusion out there, and GOG tried to refine that. But they refined it by saying use the ideal weight, use serum creatinine of 0.6. This is not going to improve the situation."

The Cancer Letter invited Smith to write a guest editorial about the controversy. It appears on page 4.

"I support the recommendations of CTEP in the absence of data," said Mark Ratain, the Leon O. Jacobson Professor of Medicine at the University of Chicago and a member of the Investigational Drug Steering Committee of CTEP.

Smith's findings are consistent with prior data, he said. "Namely, you get different results with strict application of the formula versus varying methods to reduce variability which may or may not improve accuracy."

CTEP's Ivy said the institute plans to approach the problem fundamentally, by casting away as many untested assumptions as possible. "We are not going to change the cap," Ivy said. "Until we have evidence based method for determining carboplatin dose—and in the interest of safety—we felt that this was the best approach to take at this point in time."

FDA Statement To Oncologists

The following is the text of the Oct. 8 statement to ASCO members by FDA Office of Oncology Drug Products Director Richard Pazdur:

This communication is to inform members of the oncology community of recent changes in the measurement of serum creatinine which may have an impact on carboplatin dosing. Based on preliminary communications with the National Cancer Institute/ Cancer Therapy Evaluation Program, a potential safety issue with carboplatin dosing has been identified. By the end of 2010, all clinical laboratories in the US will use the new standardized Isotope Dilution Mass Spectrometry (IDMS) method to measure serum creatinine.

The IDMS method appears to underestimate serum creatinine values compared to older methods when the serum creatinine values are relatively low (e.g., ~0.7 mg/dL). Measurement of serum creatinine by the IDMS-method could result in an overestimation of the Glomerular Filtration Rate (GFR) in some patients with normal renal function. If the total carboplatin dose is calculated based on IDMS-measured serum creatinine using the Calvert formula, carboplatin dosing could be higher than desired and could result in increased drug-related toxicity.

The current label for carboplatin provides safe dosing instructions that are based on actual GFR measurements. Provided that actual GFR measurements are made to assess renal function, carboplatin can be safely dosed according to the instructions described in the label.

If a patient's GFR is estimated based on serum creatinine measurements by the IDMS method, FDA recommends that physicians consider capping the dose of carboplatin for desired exposure (AUC) to avoid potential toxicity due to overdosing. Based on the Calvert formula described in the carboplatin label, the maximum doses can be calculated as:

Total Carboplatin Dose (mg) = (target AUC) x (GFR +25) [Calvert formula]

Maximum Carboplatin Dose (mg) = target AUC (mg•min/mL) x (150 mL/min)

The maximum dose is based on a GFR estimate that is capped at 125 mL/min for patients with normal renal function. No higher estimated GFR values should be used.

For a target AUC = 6, the maximum dose is 6 x 150 = 900 mg

For a target AUC = 5, the maximum dose is 5 x 150 = 750 mg

For a target AUC = 4, the maximum dose is 4 x 150 = 600 mg

Principal investigators of ongoing clinical trials should assess whether carboplatin dosing in those trials should be adjusted according to the above information.

Guest Editorial:

Pharmacologist Questions NCI's Short-Term Remedy For Carboplatin Dosing

By Judith Smith

The author is an associate professor and director, pharmacology research, Department of Gynecologic Oncology& Reproductive Sciences, MD Anderson Cancer Center.

Carboplatin is an ubiquitously employed therapeutic in cancer management, yet dosing is highly variable due to inconsistent measures of estimated renal function. Although the implementation of the IDMS assay for determining serum creatinine has improved sensitivity and earlier detection of chronic kidney disease, it has add yet another caveat to the equations for estimating

renal function for drug dosing. The recent Action Letter released from NCI/CTEP addressed the impact on dosing carboplatin, raising concerns for increased risk of drug-related toxicity.

Because carboplatin is renally cleared, it became apparent that dosing based on GFR might translate into better control of drug-related toxicity, specifically myelosuppression. The Calvert formula [Dose=AUC x (GFR +25)] for dosing carboplatin has been common practice in oncology. Good correlation was seen between dose and toxicity based on this method. Further, a dose-response curve identified a range of AUC dosing that was efficacious with manageable toxicity. This has been incorporated into most therapeutic regimens with the agent. The main variable in the Calvert formula is the glomerular filtration rate (GFR) which unfortunately is not readily available in clinical practice. Nevertheless, multiple equations have been developed to estimate creatinine clearance. The most common is the Cockcroft-Gault (C-G) equation ((140-age)*weight/72*SrCr)) [note *0.85 for women].

Both weight and serum creatinine are dependent upon body composition, and are two key elements that frame the difficulties in standardizing dosing recommendations. This is particularly relevant at the spectral ends of weight and serum creatinine values. In current clinical practice, there is much debate focused on both of these parameters. Many clinicians are quite frustrated by the conflicting recommendations of what body weight to be used or if/when to use an assigned serum creatinine.

Further complicating a consensus has been the implementation of the IDMS assay. The IDMS assay was introduced by the National Kidney Disease Education Program to standardize variability in serum creatinine assays, provide a more accurate measurement of serum creatinine and ultimate allow for earlier detection of chronic kidney disease.

It is clear the parameters selected for this revised assay had significant influence on estimated CrCl, particularly when estimated by the CG equation. To evaluate the magnitude of impact, we designed a retrospective assessment of carboplatin dosing in newly diagnosed, refractory, or recurrent ovarian cancer patients that received at least one cycle of carboplatin. Our goal was to determine the frequency of assigned vs. actual SrCr used in this calculation, as well as, ideal vs. actual vs. adjusted body weight. We also evaluated treatment-related toxicity, and in newly diagnosed patients, time to progression. Patients on investigational chemotherapy protocols were excluded from the study.

A total of 299 patients have been identified via pharmacy database that received at least one cycle of carboplatin between July 2002 and November 2006 in the gynecologic oncology center. The protocol was amended to evaluate an additional 100 patients between November 2008 through January 2009 compared to June 2009 to December 2009 to determine what if any impact transition period to the IDMS assay and then standardization of parameters to estimate CrCl for carboplatin dosing. Data analysis should be complete January 2011.

The results of this study will be important as it will evaluate the impact of dosing parameters on toxicity and outcome. Furthermore, we aim to quantify the difference in carboplatin toxicity, if any, associated with implementation of the IDMS assay at our institution.

After the NCI/CTEP letter was received, a snap shot cycle one data analysis was completed and submitted to NCI/CTEP for secondary review and comment. Table 1 presents a brief comparative summary of dosing stratified by IDMS vs. Non-IDMS determined serum creatinine; adjusted vs. ideal body weight, and as recommended in the Action Letter addendum from the GOG an assigned SrCr of 0.6 mg/dL vs. 0.8 mg/dL (most common in clinical practice), provided to CTEP/NCI.

Based on our own observations and from discussions on listserv and clinical forums, it was apparent that many have not incorporated the original GOG recommendations to convert to non-IDMS SrCr when estimating GFR in protocol specified carboplatin dosing algorithms.

In fact, in many instances, practitioners were unaware that their own in-house laboratory standard for serum creatinine had changed. The potential impact of this oversight has not been well elucidated. However, it is clear NCI/CTEP is concerned non-standardized and incorrect dosing has led to higher than anticipated drug-related toxicity. In our evaluation the variances in carboplatin doses are at minimum 9-12% higher.

When actual body weight is used in obese patients the carboplatin doses have been anywhere from 6.4 % up to 47% higher, which intuitively will contribute to more potential carboplatin-related toxicity.

The lower the threshold for an assigned SrCr the greater the potential for increasing risk toxicity as we observed carboplatin doses were 17 to 21% higher when assigned SrCr of 0.6 mg/dL was used in place of assigned SrCr of 0.8 mg/dL, again leading to potential increased toxicity. We have observed this is not always acute toxicity but more subtle, cumulative toxicity that

Table 1:
Demonstrating the Variability in Carboplatin Dosing based on selection of patient dosing parameters

	Mean Percent Difference in dose % (+/- Stdev)	Range of variability	
IDMS vs. Non-IDMS	9.5% (1.5%)	(4-12.7%)	Using IDMS SrCr results higher carboplatin total dose.
AdjBW vs. IBW	15.6% (7)	(6.4-47.9%)	Using IBW instead of AdjBW results lower carboplatin total dose
Assigned SrCr of 0.6 mg/dL vs. o.8 mg/dL	19.7% (0.7%)	(17.2 -21.4%)	Using assigned SrCr of 0.6 mg compared to 0.8 results higher carboplatin total dose.
AdjBW and Assigned SrCr	26.2% (6.5%)	(21-44.6%)	Using ABW instead of AdjBW and actual Sr Cr instead of assigned (combination) results higher carboplatin total dose.

occurs over the 6-8 cycles of carboplatin.

I agree there is no "best" way that will be as accurate as an actual measured GFR. Moreover, I think we all recognize that no tool is perfect, and every clinician will have an argument as to why his or her own approach is best; it is likely there is a publication to support each scenario.

However, there is much to be gained in standardizing our assessment technique. This is particularly important developing dose modification recommendations and in cross trial assessment of treatment emergent toxicity. While definition and implementation of a new algorithm will take time to reach standard practice, it is important recognize that the impact of this assessment reaches far beyond a relatively tolerant dosed agent such as carboplatin. In particular, the importance of accurate GFR estimation is considerable for agents such as cisplatin, topotecan, or pemetrexed.

The undue risk to oncology patient care due to a lack of consistency can be easily remedied.

At this time, there is a need to establish consistency in practice so that estimate CrCl calculated in XYZ major cancer center is the same, reproducible estimate when calculated at ABC community oncology practice office. Consistency between what is done during clinical trials and clinical practice needs to be established, long overdue.

The IDMS assay has established consistency in the measured results for serum creatinine. However, a consensus on what weight to use, specifically in obese patients, if and how to convert IDMS to non-IDMS serum creatinine, and what is lower threshold for SrCr to be used needs to be decided, implemented and universally adapted in a timely fashion into clinical practice to limit risk of avoidable drug related toxicity.

The ongoing study at our institution was initiated to not only look at impact of variability of parameters but also the ultimate impact on acute and chronic toxicity and long-term outcomes such as progression free survival.

Based on our snap shot preliminary data, recommendations submitted for consideration included:

• To establish Cockcroft-Gault as the equation that will be used to estimate creatinine clearance for assessment of renal function for dosing chemotherapy (narrow therapeutic agents)

• To convert the reported IDMS SrCr value to the Non-IDMS SrCr based on equation released in initial letter on June 12th 2008 from Ortho Clinical Diagnostics [Non-IDMS SrCr = IDMS SrCr *1.065 + 0.067];

• When patient is obese (> 30% IBW), the adjusted body weight should be used in the CG equation; and

• Use an assigned SrCr of 0.8 mg/dL should be minimum threshold for estimating renal function at all institutions/practices.

We anxiously await the review and feedback from NCI/CTEP on the next steps to move forward to determine the best approach for assessing renal function for dosing chemotherapy.

Obituary:

Joan Mauer, NCI Clinical Trials Auditing Expert, Dead At 65

JOAN K. MAUER, an expert in clinical trials auditing at NCI, died Oct. 10 of unknown causes at her home in Falls Church, Va. She was 65.

Mauer served in the NCI Cancer Therapy Evaluation Program beginning in 1983, at a time of intense Congressional hearings on the state of NCI clinical trials monitoring.

Mauer implemented an auditing system that has been adapted over the years for NCI-sponsored cancer centers, cooperative groups, and early phase clinical trials. She was admired for her unflappable approach, tireless devotion, calm demeanor, and sense of fairness, said Dan Hoth, who was chief of the Investigational Drug Branch at the time.

Mauer was head of the Quality and Assurance Section from 1993 until she was promoted to chief of the Clinical Trials Monitoring Branch in 2000. While creating the procedures for maintaining records and conducting audits, she viewed the audit program as a chance to educate researchers on proper clinical trials method, emphasizing the need for attentive record-keeping.

The quality assurance program that evolved under her tutelage currently conducts over 1,100 audits annually. Mauer was viewed as a prime resource to the intramural and extramural communities for compliance, regulatory guidance, and problem solving.

Her expertise and experience was invaluable in helping to start the NCI Central Institutional Review Board, and she was instrumental in beginning NCI's program to coordinate cooperative group audits using the Cancer Trials Support Unit.

"Joan will be missed terribly by the staff at NCI and by her many friends in the extramural community," said Jeff Abrams, head of CTEP. "She was the 'enforcer' of sound clinical trials practices both inside and outside the NCI, but she always came across as fair and caring, which made her admonitions all the more difficult to ignore."

Prior to joining NCI, Mauer worked at Hoffmann-La Roche for 13 years, in the Department of Medical Oncology and Immunology. She monitored and worked on the first clinical trials testing interferon and other biologic response modifiers.

Mauer received a Bachelor of Science degree in medical technology from Moravian College, and was licensed by the American Society of Clinical Pathologists. She was the recipient of numerous NIH merit awards, NCI Special Achievement Awards and a number of performance awards.

She is survived by her son Jason Mauer; sister Lynn Krueger; and two nieces.

In the Cancer Centers:

Vanderbilt Wins $7.6 Million For Prostate Cancer Study

(Continued from page 1)

the Regulatory and Ethics Knowledge and Research Program and professor of emergency medicine at the University of California, Los Angeles.

VANDERBILT-INGRAM CANCER CENTER has received a $7.6 million American Recovery and Reinvestment Act of 2009 stimulus grant to coordinate a study comparing the effectiveness of various treatments for prostate cancer. **David Penson**, professor of urologic surgery, will serve as principal investigator for the Comparative Effectiveness Analysis of Surgery and Radiation (CEASAR) study. **Daniel Barocas**, assistant professor of urologic surgery, and **Tatsuki Koyama**, assistant professor of biostatistics, will serve as co-investigators.

Vanderbilt will coordinate the CEASAR study which involves five other clinical sites, including University of Southern California, Emory University, University of California San Francisco, University of Medicine and Dentistry New Jersey, and Louisiana State University, two research methodology sites at University of California Irvine and MD Anderson Cancer Center, and a team of consultants.

CEASAR will use a network of state and city tumor registries and a national disease registry to enroll 4,200 men who were just diagnosed with localized prostate cancer and will follow their cases for a year. The researchers will collect key patient-reported outcomes, such as health-related quality of life and side-effects of therapy. The investigators also will collect clinical data, including technical details of treatment, complications, short-term cancer recurrence rates and quality-of-care indicators.

MEDICAL COLLEGE OF WISCONSIN received a five-year, $1.5 million grant from NCI to develop targeted therapies and imaging probes to detect breast cancer and its response to therapy in preclinical animal models. **Balaraman Kalyanaraman**, the Harry R. & Angeline E. Quadracci Professor in Parkinson's

Research and chairman of biophysics, is the principal investigator. Kalyanaraman, along with **Joy Joseph**, associate professor of biophysics, and other members of the research team have created mitochondria-targeted antioxidants to enhance the antitumor effect of doxorubicin while potentially reducing cardiotoxicity.

UNIVERSITY OF KANSAS MEDICAL CENTER researchers have been awarded more than $4.4 million from NIH to improve prevention and the odds of surviving cancer for rural Latino and American Indian communities in Kansas. A group of scientists at KU Medical Center has spent years establishing partnerships with Latino and American Indian communities throughout the states, leading to culturally appropriate health initiatives. With this new award, researchers will capitalize on these relationships to create the Kansas Community Cancer Health Disparities Network to address the needs of populations that are drastically underserved. **Allen Greiner**, associate professor of family medicine, is the principal investigator.

WINSHIP CANCER INSTITUTE of Emory University named **Jeanne Kowalski** director of biostatistics and bioinformatics. Kowalski will also serve as associate professor of biostatistics for Rollins School of Public Health.

Kowalski joins Emory from the Sidney Kimmel Cancer Center at Johns Hopkins where she held a faculty appointment as associate professor in oncology biostatistics, with a joint appointment in the Department of Biostatistics at the Bloomberg School of Public Health. She is the recent recipient of a Leukemia & Lymphoma Society translational grant to support her efforts in cancer stem cell clinical trial design and analyses.

EMORY UNIVERSITY'S Graduate Division of Biological and Biomedical Science, in partnership with Winship Cancer Institute, is creating a new doctoral program in cancer biology and will begin accepting students in the spring of 2011 for fall enrollment.

The graduate program will provide students with the ability to focus course work and training in all domains of cancer research. Although graduate students have been able to work in laboratories at Emory specializing in cancer, organizers expect the new program to expand training and research opportunities. **Erwin Van Meir**, professor of neurosurgery and hematology and medical oncology, is the program's founding director.

Professional Societies:

Society Honors Research Teams In Cancer Immunotherapy

International Society for Biological Therapy of Cancer honored leading research teams and individual investigators who have made significant contributions to the field of cancer immunotherapy at its annual meeting earlier this month in Washington, D.C.

Six research teams were recognized:

• Cytokine Working Group, for fruitful investigations in interleukin-2 and other immunostimulatory cytokines in the treatment of cancer, including renal cell carcinoma. Award accepted for the team by **Michael Atkins**, Beth Israel Deaconess Medical Center.

• Ludwig Institute For Cancer Research, Brussels Branch of Human Cancer Cell Genetics, for sustained efforts to describe molecular features and distribution of human tumor antigens that have led to the first target-specific clinical trial of vaccination with MAGE-3 peptides. Award accepted for the team by **Pierre Coulie** and **Pierre van der Bruggen**.

• NCI-Frederick, Biological Response Modifiers Program, for ongoing clinical and basic research that has advanced the understanding of the biological response to cancer therapies designed to modulate the human immune response. Award accepted for the team by **Robert Wiltrout**.

• NCI Surgery Branch, for their pioneering role in the development of T cell therapies for patients with cancer. Award accepted for the team by **Steven Rosenberg**.

• University of Pittsburgh, for groundbreaking work in cancer immunotherapy that has included seminal research with natural killer cells and dendritic cells, cytokines, including interferon, IL-2, tumor necrosis factor and IL-12, cancer vaccines, gene therapy, antibody therapy, immune trafficking, the tumor microenviromnent and immune monitoring. Award accepted for the team by **Ronald Herberman**.

• University of Washington Fred Hutchinson Cancer Research Center, for leading a revolution to demonstrate the feasibility and develop the enormous potential of T cell-based immunotherapies to treat and cure cancer, even in advanced stages. Award accepted for the team by **Philip Greenberg**, **Martin "Mac" Cheever**, and **Alexander Fefer** (posthumously).

The Richard V. Smalley Memorial Award was presented to **James Allison**, of Memorial Sloan-Kettering Cancer Center, pioneer in the development of a treatment for melanoma known as CTLA-4 blockade.