MEETING SUMMARY
PRESIDENT'S CANCEL PANEL
TRANSLATING RESEARCH TO REDUCE THE BURDEN OF CANCER

September 27, 2004
Columbus, OH

OVERVIEW

The purpose of the meeting, the second of four regional meetings, was to examine barriers to progress in translating cancer research into reductions in suffering and death due to cancer. The President's Cancer Panel (PCP, the Panel) is seeking input to help develop its recommendations to the President of the United States, the U.S. Congress, the Secretary of Health and Human Services (HHS), and the broader community of researchers, policy makers, advocates, and others.

PARTICIPANTS

President's Cancer Panel (PCP)

LaSalle D. Leffall, Jr., M.D., F.A.C.S., Chair

Margaret Kripke, Ph.D.

Lance Armstrong

National Cancer Institute (NCI), National Institutes of Health (NIH)

Maureen O. Wilson, Ph.D., Assistant Director, NCI, and Executive Secretary, PCP

Sarah Birckhead, M.S.W., Special Assistant, Office of the Director, NCI

Heather Kapp, M.S.W., M.P.H., Communications Fellow, PCP

Karen Parker, M.S.W., Special Assistant, PCP

David Pugach, J.D., Legislative Analyst, NCI

Abby Sandler, Ph.D., IRO, NCI

Speakers

Lucile Adams-Campbell, Ph.D., Director and Professor of Medicine, Howard University Cancer Center

Bill Bro, CEO, Kidney Cancer Association

Michael A. Caligiuri, M.D., Professor and Director, The Ohio State University Comprehensive Cancer Center–Arthur G. James Cancer Hospital and Richard J. Solove Research Institute

Mark Clanton, M.D., M.P.H., Deputy Director, Cancer Care and Delivery Systems, National Cancer Institute

Robert L. Comis, M.D., President and Chairman, Coalition of National Cancer Cooperative Groups/Group Chair, Eastern Cooperative Oncology Group

Stanton Gerson, M.D., Director, Case Comprehensive Cancer Center and Ireland Cancer Center of University Hospitals of Cleveland, Case Western Reserve University

Gary Gordon, M.D., Ph.D., Divisional Vice President, Global Oncology Development, Abbott Laboratories

Scott Gottlieb, M.D., Senior Advisor to the Administrator, Centers for Medicare and Medicaid Services

Michael R. Grever, M.D., Associate Dean for Medical Services, Professor and Chair, Department of Internal Medicine, The Ohio State University Medical Center

Catherine D. Harvey, R.N., Dr.P.H., AOCN, Chair, Board of Directors, National Coalition for Cancer Survivorship

Ronald B. Herberman, M.D., Director, University of Pittsburgh Cancer Institute

Clifton Leaf, Executive Editor, *FORTUNE* Magazine

Homer L. Pearce, Ph.D., Distinguished Research Fellow, Eli Lilly and Company

Stephen M. Prescott, M.D., Executive Director, Huntsman Cancer Institute

Eddie Reed, M.D., Director, Mary Babb Randolph Cancer Center

Paul L. Schaefer, M.D., Principal Investigator, Toledo Community Oncology Program

Harold C. Sox, Jr., M.D., Editor, *Annals of Internal Medicine*

K. "Vish" Viswanath, Ph.D., Associate Professor of Medical Oncology, Center for Community-Based Research, Dana-Farber Cancer Institute

Steven N. Wolff, M.D., Professor of Medicine, Meharry Medical College

Lisa J. Zimmerman, M.S., Director, Quality Assurance and Regulatory Compliance, Duke Clinical Research Institute

OPENING REMARKS—DR. LaSALLE D. LEFFALL, JR.

On behalf of the PCP, Dr. Leffall welcomed invited participants and the public. He provided a brief overview of the history and purpose of the Panel and the aims of the current series of meetings on translating research to reduce the burden of cancer. Dr. Leffall explained that the meeting would consist of three panel discussions, each addressing a unique aspect of translating research. Abstracts submitted in advance by the speakers were made available during the meeting.

WELCOME—DR. MICHAEL CALIGIURI

Background

Dr. Caligiuri is the Director of the Division of Hematology and Oncology in the Department of Internal Medicine at The Ohio State University (OSU). Holder of the John L. Marakas Nationwide Insurance Enterprise Foundation Chair in Cancer Research, he serves as Director of the Comprehensive Cancer Center (CCC) of The Ohio State University and Deputy Director of the James Cancer Hospital and Solove Research Institute. Dr. Caligiuri received his doctorate in Medicine from Stanford University School of Medicine.

Key Points

- The Ohio State University is the largest university in the United States and has one of the most comprehensive health sciences campuses in the country, as well as an NCI-designated Comprehensive Cancer Center. Recently, the Board of Trustees moved toward approving a $400 million program that will double the size of the cancer program, focusing on three areas: human cancer genetics, experimental therapeutics, and prevention. This program will also bring in nearly 100 new investigators and create approximately 1 million square feet of space.
- It is important to create public awareness about the importance of reducing the cancer burden. Dr. Caligiuri and Dr. David Schuler, Executive Director of the James Cancer Hospital, have worked together to develop programs to that end, including improving the Comprehensive Cancer Center and promoting an outreach program in southern Ohio focused on reducing the incidence of cervical cancer.

PANEL DISCUSSION I—BARRIERS TO TRANSLATING RESEARCH INTO REDUCTIONS IN THE BURDEN OF CANCER

INTRODUCTION—DR. MARK CLANTON

Background

Dr. Clanton is currently the Deputy Director for Cancer Care and Delivery Systems at the National Cancer Institute (NCI), with responsibility to increase the impact of the Institute on the quality and cost and reimbursement of cancer care, as well as to provide leadership in the national effort to reduce cancer health disparities. Prior to joining NCI, Dr. Clanton was President-Elect of the American Cancer Society (ACS). In 2003, he served on the National Cancer Institute External Work Group for *Cancer Progress Report 2004* and the Harvard School of Public Health Leadership Council. Dr. Clanton completed his medical training at Tulane University Medical School and the Texas Children's Hospital in Houston.

Key Points

- NCI and the U.S. Food and Drug Administration (FDA) have developed a relationship with the goal of aiding the FDA approval process by electronically sharing information about NCI clinical trials of new drugs. Likewise, the Centers for Medicare and Medicaid Services (CMS) and NCI work together to develop quicker clinical trials and payment processes regarding off-label uses of drugs. The goal is to have all three agencies—NCI, CMS, and FDA—working together to acquire information about what works and what makes sense, as well as how to ensure that decision makers receive that information.

MR. CLIFTON LEAF

Background

Clifton Leaf is the Executive Editor of *FORTUNE* magazine, where he helps oversee the magazine's editorial coverage and staff in addition to directing *FORTUNE's* Wall Street and investing coverage. Mr. Leaf has written nearly a dozen articles for the magazine, including his provocative analysis on the War on Cancer: "Why We're Losing the War on Cancer (and How to Win It)." Prior to joining the staff of *FORTUNE*, Mr. Leaf was Executive Editor of *SmartMoney*, where his writing shared a nomination for the National Magazine Award. Mr. Leaf has also written for *The New York Times* and many other national publications and held editorial positions at *fitness* magazine and *Harper's BAZAAR*. Mr. Leaf received his Master of Fine Arts degree in Writing from Sarah Lawrence College.

Key Points

- Three-quarters of the cancer drugs approved by the FDA between January 1990 and November 2002 do no more to keep people alive than the standard treatments in use. In half of the cases, the primary basis for approval was a partial tumor-response rate. However, in 90 percent of cancer deaths, the process of metastasis, rather than the initial tumor, is the cause of death. Many of the cancer drugs approved by the FDA do not combat metastases, though they may improve quality of life or increase time to progression of the disease.
- During the same 1990–2002 period, English-language newspapers reported "cancer breakthroughs" in 691 separate articles. The perception is that progress is being made in the fight against cancer, but the drugs being developed do not actually fight cancer in a way that leads to higher survival rates. The cancer community's overuse of medical jargon also contributes to this misperception.
- Misleading statistics also obscure how many people are developing and dying of cancer. The age-adjusted death rates the cancer community relies upon to measure progress over time do not measure the actual change in death toll. Because the American population has been aging as it grows, the

cancer rate has increased. Age-adjusted death rates do not reflect the aging population; there are actually more people dying of cancer than the age-adjusted rates show.

- The annual cost of cancer treatment will exceed $94 billion in 2014. Americans will spend $800 billion on cancer treatment in the next decade.
- The cancer community has become so focused on specialization that it is difficult for researchers to communicate across specialties. Using plain language instead of scientific jargon would enhance the solicitation of feedback from researchers in other specialties. Likewise, this would provide a richer basis for applied and collaborative research.
- The lay press is culpable as well and has misguided the public in its search for and presentation of early medical breakthroughs.

DR. SCOTT GOTTLIEB

Background

Dr. Scott Gottlieb is a physician and Senior Advisor for Medical Technology to Mark McClellan, Administrator of the Centers for Medicare and Medicaid Services (CMS). Prior to joining CMS, Dr. Gottlieb was Director of Medical Policy Development at the U.S. Food and Drug Administration (FDA). He has served on the editorial staff of the *Journal of the American Medical Association* and the *British Medical Journal* and writes frequently on topics of health care, politics, and culture for *The New York Times*, *The Wall Street Journal, USA Today*, the *Los Angeles Times,* and other publications. Dr. Gottlieb is a graduate of the Mount Sinai School of Medicine.

Key Points

- CMS recognizes the important role off-label use of cancer drugs plays in personalizing cancer treatment, giving doctors the ability to tailor regimens to specific tumor types and individual patients. More and more treatments now being used represent those highly personalized regimens. CMS is looking for ways to encourage the development of better information around the general use of cancer drugs and in the off-label setting in particular.
- CMS is not looking for ways to stop paying for off-label use of cancer drugs; recent media reports to the contrary are inaccurate. CMS is required by law to pay for all on-label use of cancer drugs as well as all uses that are specified in certain compendia of drug treatments, including off-label uses. Legislation does not require CMS to pay for off-label uses not listed in the compendia. Traditionally, CMS has let local carriers make local decisions about payment for such unlisted uses. This has led to much disparity across the country: some carriers will pay for all uses of a new cancer drug, and some will pay only for what is provided by the law. It is reasonable to expect a CMS policy of coverage for all labeled uses, off-label uses listed in compendia, and some unlisted off-label uses for which information can be collected.
- CMS needs to move away from the paradigm of global reimbursement decision making for new drugs and toward a paradigm of local decision making, empowering local hospitals, local regions, individual doctors, and patients. There is opportunity under the new Medicare law to contribute to the development of better information that can help guide such decisions. The new law provides funding for comparative-effectiveness studies of new treatments; funding for oral replacement therapies; new authority and resources for participation in development of clinical trials, clinical studies, and, in particular, practical clinical studies; and establishment of the Council on Technology and Innovation, which gives CMS new authority and resources to specifically target new technologies and develop guidelines to speed the reimbursement process for new drugs.
- There are real opportunities in the FDA-CMS relationship, but there are also challenges. One of the opportunities is in allowing CMS access to data earlier in the FDA clinical trials process so that when an approval decision is made, CMS will be ready to make a reimbursement decision quickly, and reimbursement will not become an obstacle to obtaining access to the drug. One challenge, however,

lies in the same process. Drug developers may be concerned that the FDA reviewer will perceive the exchange of information between FDA and CMS as pushing the approval process. Another challenge is that clinical trials should not be designed based on future reimbursement considerations. Adding mandates for new information requirements to the FDA approval process for the sole purpose of guaranteeing reimbursement would invariably delay access to the drug.

- Recently, CMS changed its payment for infused cancer drugs to more accurately reflect the true price of those drugs in the marketplace, which is significantly less than CMS has historically paid. Clinicians had used the excess payment to cover the cost of administering the drugs. CMS is now attempting to pay a true price for the drugs themselves and a true price that reflects the cost of administration. CMS has been talking closely with the American Society of Clinical Oncology (ASCO) and others in the cancer clinical community to reach a resolution that all stakeholders can accept.

DR. MICHAEL R. GREVER

Background

Dr. Grever is the Associate Dean for Medical Services at The Ohio State University Medical Center, Chairman of the Department of Internal Medicine, and the Charles A. Doan Chairman of Medicine. He is also a Professor of Medicine and Program Co-Leader for Experimental Therapeutics at Ohio State's James Comprehensive Cancer Center. From 1994 to 1999, Dr. Grever was Director of the Hematologic Malignancies Division and Professor of Oncology at Johns Hopkins University School of Medicine. Dr. Grever received his M.D. from the University of Pittsburgh.

Key Points

- The majority of drugs in current use has been discovered through the empiric screening approach, and many are derivatives of natural products, such as the bark of the yew tree (Taxol), or from "broths" of bacterial cultures, among others.
- No fatal disease has been successfully addressed without using a combination of strategies to circumvent diverse mechanisms of resistance. Underestimating the importance of new agents for fatal disease treatment would drastically alter the potential for improving survival. The only way to increase the number of complete remissions and see improvement in survival is to use combination strategies.
- In the early 1990s, Dr. Anthony Fauci mandated that the drug development process for patients with fatal diseases be expedited. While the initial intention was to help patients with HIV, many benefits have been shared by the cancer patient population.
- First trials in man are critically important, and no hint of activity should be underestimated. Ninety-five percent of all the drugs introduced into humans at NCI are introduced very safely.
- The Government must remain committed to the drug development process. NCI has been a stalwart supporter of cancer drug development—as well as anti-HIV therapies—which would not be possible were it accountable to investors as are others in the industry.
- One challenge in drug development is the lack of communication between the scientific and physician communities. Forming teams is one way to shorten the preclinical drug development program. In the university setting, having adequate mentorship for new physician-scientists is important. Also, NIH K23 grants allow a physician-scientist who wants to be a clinical investigator to partner with a basic scientist as a mentor. R21 grants for translational research also provide funding for basic scientists, thus aiding the scientist who is not in a university setting, where most rewards, such as tenure and promotion, exist.
- Another challenge in this process is the lack of time available to simultaneously mentor researchers, serve patients, provide education, and target clinical research. There are also increasing restrictions

regarding appropriate hours for trainees in hospitals. Junior faculty are burdened with long hours and still do not have enough time to do everything.

- The greatest obstacle to drug development and delivery is the disease process itself. The greatest opportunities, though, lie in people keeping faith and exercising patience. Important treatments would be lost if patience in the development process were lost. Persistence is critically important.

DR. HOMER PEARCE

Background

Dr. Homer Pearce is a Distinguished Research Fellow in Cancer Research at Lilly Research Laboratories, Eli Lilly and Company. Previously, Dr. Pearce was Vice President of Cancer Research and Clinical Investigation at Lilly. He is a member of the American Association for Cancer Research, American Chemical Society, American Association for the Advancement of Science, and C-Change. Dr. Pearce received his Ph.D. in Organic Chemistry from Harvard University.

Key Points

- During the last 25 years, there has been a revolution in the knowledge of cancer as a disease process that is beginning to be understood on both a genetic and biochemical level. This new understanding is creating new opportunities for the cancer drug industry to discover medicines and other disease interventions that will be far more effective than past attempts to treat patients.
- Cancer will soon overtake heart disease as the leading cause of death in the United States. One of the reasons that advanced cancer is so hard to treat is that a metastatic tumor has undergone a complex and heterogeneous process of transformation. The clinical manifestation of this advanced disease may be too complex to cure or even treat effectively; intervening in the early stages of the disease process—before the tumor becomes hopelessly complex and spreads—may provide the best opportunity to reduce cancer deaths.
- It is not clear that early pharmaceutical intervention in the disease process—also known as *chemoprevention*—will ever become a real option for individuals at risk of developing cancer. To bring a new chemoprevention drug to physicians and their patients, there are a number of substantial impediments to overcome. First, there are developmental challenges. Even with treatment study commitments, the true risk/benefit ratio of chemoprevention drugs is hard to demonstrate. Second, the time required to develop a cancer chemoprevention drug quickly erodes available patent life that enables the private sector to fund these high-risk research and development investments. The U.S. system of intellectual property protection significantly discourages clinical trials research in the development of chemoprevention alternatives. Also, it is important to have a methodology to identify patients who are at risk. Therapies must be delivered in a way that is sensitive to the molecular structure of the disease, using different treatment regimens.
- As technology evolves, the medical community will have access to malignancy biomarkers, which will help doctors take preventive measures. Other technologies will also be needed.
- There will also need to be significant public education at the national level; this is an effort with which the press can help. Once cancer is understood as a disease process rather than as a diagnosis at a point in time, participation in prevention efforts—even lifestyle modifications—would be much more likely.
- A partnership needs to be formed among industry, regulators, Congress, patient advocates, and other key stakeholders—like the NCI—with the goal of reforming the process by which prevention drugs are brought before the FDA and reviewed. This means a new system for approving prevention indications that actively encourages prevention research. There is yet to be meaningful change in the current system; the Panel could play a role in encouraging change.

- The greatest current opportunity for information about cancer and cancer drugs to be communicated to patients lies in the public education system. It would be very easy to begin reframing public school education to include information about cancer as a disease process.

MS. LISA ZIMMERMAN

Background

Lisa Zimmerman is Director of Quality Assurance and Regulatory Compliance at Duke Clinical Research Institute (DCRI). Ms. Zimmerman's main areas of focus have been regulation and compliance. In her tenure at DCRI, she has developed a Quality Assurance and Regulatory Affairs department and has spearheaded a number of initiatives consistent with that academic mission. Ms. Zimmerman has also been involved with *The New Jersey Governor's Conference on Effective Partnering in Cancer Research*, Health Insurance Portability and Accessibility Act (HIPAA) privacy laws and how they shape the future of research, and a host of other projects in different subject areas.

Key Points

- There has been a significant increase in spending on biomedical research in the past 10 years, but output of new products has declined since 1997. Fifty percent of applications fail in the Phase III stage of clinical trials; according to a 2003 FDA report, cancer drugs have more late-stage Phase III study failures than most other therapies. These failures drive up the price of successfully bringing a new drug to market, currently estimated at about $802 million.
- The cancer research process is essentially broken. The system is reactive rather than proactive; it is time to change the system to a proactive one. Major barriers to change include the inability to share information between and among scientists and researchers; lack of training available to researchers who design and conduct clinical research; lack of education available to mentors who are responsible for educating others; lack of support systems at the university level; and lack of support systems at NCI for those navigating the regulatory pathways.
- Steps toward overcoming systemic challenges include allowing the FDA to share information about cancer trials and why they fail; managing and effectively using the volumes of available information about disease and the regulatory pathway, as well as local and Federal regulations that impact research; and creating common goals, frameworks, and avenues of communication. Only then can drugs begin to be sped to market at reduced costs.
- Those in academia works very hard to receive NIH grants, build relationships, and work on current "hot buttons," but they are not educated about regulatory processes. Here again, communication and education would benefit the system.
- Coordination of academic grants and industry funding is very difficult. Each institution has its own set of regulations and processes. The institutional review board (IRB) process is also difficult to maneuver, as each IRB has its own process for approval. A meeting of IRB members to discuss how to make tough decisions is strongly encouraged.
- These problems persist when academic centers work with community centers to run clinical trials. Many community centers are not educated about trial and regulatory processes. Because of cost concerns, DCRI has decided that the regulatory group will operate on a volunteer basis to assist investigators.

MR. WILLIAM BRO

Background

Mr. Bro is Chief Executive Officer (CEO) of the Kidney Cancer Association, which serves 60,000 constituents in the United States and 90 other countries. He is a past Chair of the Association, having succeeded the organization's founder, Eugene P. Schonfeld, and has served as its CEO since 2002.

Mr. Bro is a retired corporate executive with a 35-year background in broadcast station management, ownership, consulting, and Web site development. Mr. Bro is also a 14-year kidney cancer survivor.

Key Points

- In 1989, when Mr. Bro was diagnosed with renal cell carcinoma, there was no FDA-approved treatment and virtually no option other than surgery to treat the disease. The Kidney Cancer Association was founded by a few strongly committed kidney cancer patients with the goal of improving treatment for their disease. The Association has since been influential in the FDA decision to fast-track interleukin-2 for approval and has formed durable relationships with NCI researchers, industry, and influential politicians.
- Sometimes, discussions are so focused on current trends that the considerable effort that has already been expended becomes lost in the clutter. The substantial work of the various progress review groups (PRGs) should be acknowledged with an eye toward encouraging implementation of their recommendations. In August 2002, the Kidney/Bladder Cancers Progress Review Group submitted a report to the Director and the Advisory Committee to the Director of NCI, which accepted the Director's charge to develop a national plan for the next 5 years of kidney and bladder cancer research. If implemented, the 13 priority recommendations identified by the PRG will stimulate multidisciplinary research that can significantly advance progress, ultimately leading to discoveries that will reduce the burden of these diseases.
- The lack of participation in clinical trials needs to be addressed. With accrual rates in the range of 2 to 3 percent, it is very likely that many useful clinical trials will fail to accrue sufficient numbers to hit their targets; the public may never recognize the benefits of these novel agents. By the time an agent reaches the clinical trial stage, better mechanisms need to be in place to educate the public so that participation is improved. One step would be to improve public school education about cancer, cancer research, and why understanding cancer is important.
- The fact that there are now 160 kidney cancer clinical trials listed in the clinicaltrials.gov database indicates that there is considerable interest in kidney cancer. Patient advocate organizations have done a good job of raising awareness for "small" cancers in recent years. However, there still has been little progress toward finding a cure; there still is only one FDA-approved drug for the treatment of this disease. In order for a cure to be deployed, there must be sufficient interest by industry in finding a cure.

DR. GARY GORDON

Background

Dr. Gary Gordon is currently the Divisional Vice President for Global Oncology Development at Abbott Laboratories. Prior to joining Abbott, Dr. Gordon was Chief Scientific Officer and Vice President of Clinical Affairs at Ovation Pharmaceuticals. His professional memberships include the American Association for Cancer Research (AACR) and the American Society of Clinical Oncology (ASCO). Dr. Gordon received his Ph.D. in Pharmacology and Experimental Therapeutics from the Johns Hopkins University School of Medicine.

Key Points

- Remarks at this meeting are centered on three basic areas: communication and interaction within the oncology community, including the FDA, NCI, academia, and the Cooperative Groups; information availability, especially as it relates to the FDA and clinical trials; and prevention.
- How laboratory advances are applied in the prevention setting is particularly important and needs more attention. The cardiovascular community has made huge strides in prevention; the oncology community is considerably behind. There are ways of identifying people at risk for cancer, but new knowledge needs to be appropriately applied. For example, oral leukoplakia is a precursor lesion to various types of head and neck cancers and is relatively easy to identify in a physical examination.

The problem up to now has been identifying the type of oral leukoplakia that represents highest risk for becoming cancer. It appears that there are certain molecular characteristics that allow doctors to identify higher-risk leukoplakia; pursuing research on this lesion could be helpful in prevention program development.

- Another problem for oncology prevention is that cancer is classified anatomically. If the FDA were to abandon anatomic classification and move to molecular classification, it would aid in developing measurements in a reproducible and reliable way. Assay development might also follow.
- The biggest issue currently being faced is the inability to communicate with FDA early in the drug development process. Drug developers need to be able to communicate with the FDA without the, perhaps, irrational fear that asking questions will somehow provoke a regulatory response that creates an even bigger burden. The ability to discuss clinical trial implementation processes, particularly around data collection and quality assurance, would be very helpful. If information-sharing processes can be developed, it would be possible to reduce the $800 million-to-$1 billion drug development costs.

PANEL DISCUSSION II—THE ROLE OF ACADEMIC MEDICAL CENTERS IN TRANSLATING RESEARCH INTO CLINICAL PRACTICE

INTRODUCTION—DR. MICHAEL CALIGIURI

Dr. Caligiuri introduced the panel members.

DR. RONALD B. HERBERMAN

Background

Dr. Herberman is currently the Director of the University of Pittsburgh Cancer Institute, Associate Vice Chancellor for Cancer Research, Hillman Professor of Oncology, and a Professor of Medicine and Pathology. Most recently, he has assumed the position of Director of the University of Pittsburgh Medical Center (UPMC) Cancer Centers, a prestigious network of the UPMC Health System.

Key Points

- In order to address the challenge of effective dissemination of research advances, the University of Pittsburgh Cancer Institute and other NCI-designated Comprehensive Cancer Centers and academic medical centers have formed multidisciplinary groups that focus on a particular cancer type or a modality of treatment. The aim of these groups is to stimulate discussions, interactions, and, hopefully, collaborations across a spectrum of experts—from basic cancer researchers to clinical oncologists. Although this facilitation of translational research is critically important, it is also essential to achieve advances that occur beyond initial clinical applications and disseminate them into widespread practice.
- It is also important to foster effective interactions between academic medical centers, particularly cancer centers, and industry; NCI has been playing an important role in the academic public-private partnership program launched last year. This is a challenging area and one that merits substantially more funding support.
- The biggest challenge to dissemination lies in moving promising applications out of the academic cancer center and into the community. In response, the University of Pittsburgh Cancer Institute has been developing a hub-and-spoke model in which the Cancer Center is closely integrated and coordinated with a wide community network in the region and is responsible for central oversight and personnel training. The Cancer Center then becomes responsible for what goes on in the regional community network. The model is still in the early stages, but the indications so far are promising. More clinical research studies are being implemented in the community and more community oncologists are becoming actively involved in clinical research; in turn, those oncologists are making an impact on some of the clinical trials to increase their relevance to the problems of cancer in the community, which are often different from those in the academic center. Critical to building trust with the community oncologists is ensuring that patients who can be treated in the community are, indeed, treated in the community. Community clinical oncology representatives are included in the Cancer Center leadership.
- This kind of model does require resources. NCI, through two funded grants, is helping the Institute implement this model. Also, there has been development of a process by which the revenue from the clinical practice of oncology is generating increased efficiency, which then generates revenues that can be put back into support for infrastructure and staffing.
- Communication is very important, and the challenge requires creative approaches. Videoconferencing has proven important in facilitating effective connections between the Institute and the community it serves. Hand-held PDAs containing information about all open clinical trials and eligibility criteria are being evaluated for use by practicing clinical oncologists.

- No single cancer center has all of the relevant expertise and capabilities. The Institute has been setting up collaborations among different cancer centers, particularly those within its region. One collaboration, for example, is a consortium to evaluate biomarkers and their usefulness in predicting tumor development and clinical responses to therapy.
- Bioinformatics is aiding effective communication. NCI's recent funding for the Cancer Biomedical Informatics Grid (caBIG) is very promising; cancer centers around the country will be able to more effectively communicate with each other, receive full clinical annotation of tumor specimens, and determine whether particular biomarkers, for example, are useful for the intended purpose.
- Tumor registries merit more widespread evaluation and implementation. Registries should be built upon and converted from incidence registries to outcomes registries, which will better enable researchers to evaluate best practices and deviations from those practices.

DR. STEPHEN M. PRESCOTT

Background

Dr. Prescott is the Executive Director of the Huntsman Cancer Institute. He was a founder and the Director of the Eccles Program in Human and Molecular Biology and Genetics at the University of Utah. Currently, he is a Professor of Internal Medicine and holds the H. A. and Edna Benning Presidential Endowed Chair. Dr. Prescott received his M.D. degree from Baylor College of Medicine.

Key Points

- The Huntsman Cancer Institute serves the largest geographical region of any NCI-designated Cancer Center. The region's population is unique in that it is home to the largest concentration of Native Americans. The region also contains Utah, which was founded by the Church of Jesus Christ of Latter-day Saints (Mormons). Because of the genealogical focus of the Church, it has been possible to link much of the Mormon population in a database that when linked with the Utah cancer registry, provides a thorough description of the population's cancer incidence and outcomes. This allows researchers to look at genetic predisposition and other factors that influence the likelihood of cancer, patterns of response to treatment, and likelihood of adverse events and outcomes. More than 400 colon cancer deaths have been prevented in the last 7 years using information from these databases.
- The Utah database represents a completely European-derived population. If there are alleles that predominately affect other ethnic groups, this database will not be helpful. However, genetics investigators have discovered more than 40 disease-causing genes that have been determined to be broadly applicable to all populations, including Asian- and African-derived populations. However, it is difficult to share this database and still protect privacy as mandated by HIPAA. Understanding barriers created by HIPAA and other guidelines and exploring ways to overcome those barriers is very important.
- From a policy point of view, prevention is paramount. Understanding the genetic basis of cancer and how that information can be used to design novel biomarkers, *in vivo* imaging, and other approaches will be essential in developing an effective prevention program.
- There are a number of barriers to dissemination. First, when focusing on prevention, the wrong individuals are often considered the "front line." Instead of concentrating on high-end, specialized systems, such as cancer centers and academic medical centers, prevention begins with general internists and family practitioners, as they are the doctors doing health maintenance and screening—i.e., the "front line." Second, there are institutional barriers in many organizations, particularly academic medical centers. Academic institutions can make improvements by overhauling reward systems that highlight individual achievement over transdisciplinary teamwork. Leaders of academic centers need to build teams that span the spectrum of specialties and reward shared victories and achievements. An additional barrier is over the NIH/NCI grant system, which rewards principal investigators over inter- or transdisciplinary teams.

- There are also barriers to creating effective partnerships, especially those with the commercial sector. Partnerships tend to be based on contractual negotiations: the researcher has a deliverable, and the company has a responsibility; once the researcher has delivered his or her product, there is no more information sharing.
- Long-term support from the Federal Government and/or the pharmaceutical industry will be needed to develop new technologies and drugs.

DR. EDDIE REED

Background

Dr. Reed is the Director of the Mary Babb Randolph Cancer Center at the Robert C. Byrd Health Sciences Center, West Virginia University (WVU). His research interests are focused on gynecologic and genitourinary malignancies. Dr. Reed is also interested in viral carcinogenesis. The primary focus of his studies has been high-risk human papillomavirus (hrHPV) and its association with cervical cancer and cancers of the head and neck. Dr. Reed's laboratory recently completed an almost 800-person surveillance study involving 33 sites across the state.

Key Points

- West Virginia University serves a population that is unique in several respects. Nationally, the state of West Virginia ranks 51st in median household income, is second in median age of its residents, has the fifth highest poverty rate, and is the second most rural state. Although there are several modern metropolitan areas within West Virginia, the majority of the state is rural and has scattered resources to deal with mounting health problems and other issues.
- Two things are being done well and deserve special emphasis; both of these require continued and expanded support. The first is the Centers for Disease Control and Prevention's Breast and Cervical Cancer Early Detection Program (BCCEDP), which seeks to provide screening to women who are uninsured or underinsured. The state of West Virginia provides funds to assist individuals who are diagnosed with cancer through this screening program. West Virginia University has initiated a study of the cost-effectiveness of the program.
- There are currently several problems with the Program. First, it is not funded as well as it should be to reach the families it could easily serve. The Program should be strongly supported, and consideration should be given to expanding this program to include other major malignancies for which data suggest screening would profoundly impact the health of the population. In those malignancies for which data are incomplete, such a program could be used as a platform to conduct important clinical studies to answer critical questions about screening and its effectiveness. The application of this approach to a broader range of malignancies will be needed to make a major impact on the cancer burden in West Virginia. Also, WVU is conducting research regarding the cost effectiveness of the BCCEDP in order to demonstrate the benefits of screening to citizens and insurance companies.
- Second, the program and others like it represent unexploited opportunities to gain important new knowledge about cancer causality in real time and space. Most cancer prevention knowledge is developed using animal models, which have severe limitations in terms of applicability to the human situation. Supporting active research linking service (as occurs in the BCCEDP) to peer-reviewed research on important clinical questions that can be easily addressed in this setting is an opportunity that should be taken advantage of.
- The second thing being done right is the NCI plan to expand the number and breadth of NCI-designated Cancer Centers. The expansion of the NCI Cancer Center network is essential to the dissemination of state-of-the-art clinical care and research to all American citizens. However, limiting expansion to just one institution per year is a major mistake. Denial of NCI designation to institutions that meet the rigorous peer-review criteria is directly contradictory to the goals of reducing the nation's cancer burden.

DR. HAROLD C. SOX, JR.

Background

Dr. Sox is the Editor of the *Annals of Internal Medicine.* He also chairs the Medicare Coverage Advisory Committee of the Centers for Medicare and Medicaid Services (CMS) and serves on the Report Review Committee of the National Research Council. Dr. Sox is President of the American College of Physicians–American Society of Internal Medicine. He received his M.D. from the Harvard Medical School.

Key Points

- There are currently three barriers to successfully reducing the risk of cancer. The first is infrequency of the disease in the screened population; healthy people are by definition the targets of screening programs, and they seldom experience the target disease.
- The second barrier is that prevention is inefficient because disease is infrequent in screened populations or populations undergoing chemoprevention; most patients who undergo screening or chemoprevention do not have the target disease and will never get it. Therefore, many people are exposed to the intervention and its possible harms in order to benefit a single individual. Yet another barrier is that the rates of performing preventive services are too low.
- Some of the problems with cancer prevention occur because relatively poor technology exists for targeting people at high risk and reducing their risk. Worse, the cancer community does not consistently deliver agreed-upon important services.
- There are ways to overcome these problems. The first is to reduce the harms of screening programs. These occur because so few screened patients have or will get the target disease. Most screened patients can only suffer the harms of screening, including worrying that they have cancer and undergoing invasive, painful tests to be sure that they do not. Improving screening tests to reduce the frequency of false positive results would mean fewer people experiencing several weeks of worry followed by a negative biopsy. More accurate screening tests and safer, cheaper follow-up tests after positive screenings are needed. Academic medical centers can play a leading role in the research on this topic.
- The second way to overcome these problems is to improve the ability to identify patients who are at the highest risk for the target disease and for the complications of follow-up tests and treatment. Academic medical centers typically are the sites of the epidemiologic studies that allow researchers to stratify patients by their risk of cancer.
- The ability to deliver screening and risk-reduction services to patients should also be improved. One way is to develop electronic medical record systems for small office practices, where most care occurs. These systems can remind office staff when a patient is due for preventive services, detect when a patient has actually had the service, and connect with national data systems for tracking screening performance. Another way is to create incentives for practices to offer preventive services to a high proportion of eligible patients.
- Academic medical centers can also conduct more research on the behavioral factors that motivate physicians and patients to follow suggested guidelines regarding prevention. For example, in the smoking intervention arena, research has shown that the most important factor in influencing patients to follow through on tobacco cessation programs was a strong statement from their physicians about the dangers of tobacco. The cancer community needs to make it clearer to physicians how important they are in their patients' decisions to stop smoking. Also, patients need to be motivated by understanding that quitting tobacco use really can make a difference.
- Knowing a person's genetic endowment, as in the case of the Mormons in Utah, is one way to identify people who are at higher risk; this is supported by what is known about breast cancer. It would be easier to motivate people, for example, to stick with smoking programs if research showed

that they had a genetic polymorphism that made them more susceptible to the effects of cigarette smoking.

- Identifying and targeting high-risk people can have consequences: In breast cancer, for instance, only a small proportion of women who are at risk actually carry the genes associated with high risk. If prevention efforts focused only on women at high risk, many people at average or slightly below average risk would not be screened, even though their risk was high enough to justify screening.
- Personal knowledge of patients' histories, risk factors, and habits is a huge advantage that primary care physicians have; this helps them do their part to reduce the risk of cancer. However, physicians simply may not remember to do preventive health services in the office setting. Electronic medical records can do the job of reminding them.
- Research shows the most important factor in increasing cancer screening rates in primary care populations is scheduling a visit solely for the purpose of prevention. Primary care physicians should be more systematic about scheduling preventive service visits, and Federal agencies should find a way to reimburse them for visits devoted entirely to disease prevention and health promotion.

THE ROLE OF ACADEMIC MEDICAL CENTERS IN MOVING RESEARCH INTO COMMUNITIES—DISCUSSION

Key Points

- It is important to develop novel approaches to link academic cancer centers with the communities and regions they serve. This is one of the criteria for designation as an NCI Comprehensive Cancer Center, but it is minimally funded, at best.
- The most effective mode of cancer treatment is prevention. However, the prevention approaches that target high-risk individuals require access to medical records on a large scale. Legal barriers, including HIPAA, hinder such access-based approaches.
- Electronic medical records are the key to improving delivery of preventive health services to primary care patients and in making primary care physicians accountable for their performance. Every primary care physician should have an electronic medical record capable of supporting preventive health services. However, NIH has rules about the handling and security of electronic records that seriously impede use of electronic technology. Researchers should meet with Government agencies to decide how to use electronic records while still safeguarding privacy.
- Academic medical centers need to contribute to the research that shows that prevention reduces bottom-line costs.
- The University of Pittsburgh Cancer Institute is able to provide high-quality radiation therapy in the community. Studies conducted by the major Blue Cross insurance provider in Western Pennsylvania indicate that the farther away a community is from the urban and academic settings, the less compliance there is with recommendations for radiation therapy. Using the cancer center/community integration model, the Institute has made available not only good-quality radiation therapy, but even intensity-modulated radiation therapy (IMRT). This therapy is as available 100 miles from Pittsburgh as at the Institute itself by employing the right type of high-speed communication lines conducive to centralized radiation physics planning, which is then sent out into the community. The result is that the same IMRT can be delivered in the community as at the Center.
- NCI mandates that the Comprehensive Cancer Centers develop programs that generally consist of groups of individuals with both basic and clinical prevention expertise. The Ohio State University Comprehensive Cancer Center has found that when a Ph.D. scientist and a physician-scientist are partnered in leading those programs, the amount of translational research doubles. Appointing people who understand both basic and clinical oncology benefits patients.
- Another facet of communication that should be explored is that among cancer patients, the community, and physicians. This communication should emphasize the psychosocial and spiritual as

well as the physical burdens of cancer. There are many common links among cancers, yet they are considered to some degree to be different diseases. The stages that patients go through are much the same.

PANEL DISCUSSION III—BEST MECHANISMS FOR MOVING RESEARCH INTO COMMUNITIES

INTRODUCTION—DR. ROBERT L. COMIS

Background

Dr. Comis is President and Chairman of the Coalition of National Cancer Cooperative Groups, Inc. He is also a Professor of Medicine and Director of the Drexel University Clinical Trials Research Center in Philadelphia, as well as Group Chair of the Eastern Cooperative Oncology Group (ECOG). He currently serves on the Boards of Directors of the American Society of Clinical Oncology (ASCO), National Coalition for Cancer Research, and the American Radium Society. Dr. Comis received his medical degree from the State University of New York (SUNY) Health Science Center School of Medicine in Syracuse, New York.

Dr. Comis introduced the panel members.

DR. LUCILE ADAMS-CAMPBELL

Background

Dr. Adams-Campbell, Director of the Howard University Cancer Center, is currently the only African-American woman director of a Cancer Center in the country. She is a tenured Professor of Medicine, Graduate Professor of Psychology, and Associate Professor of Physiology and Biophysics at Howard University. She received her Ph.D. in Epidemiology from the Graduate School of Public Health at the University of Pittsburgh in 1983 and was the first African-American female in the country to receive a Ph.D. in Epidemiology.

Key Points

- Many factors contribute to cancer health disparities, including differences in socioeconomic status and health insurance coverage. However, these factors alone do not account for the differences in incidence and outcomes of disease. Unequal treatment as a result of explicit and implicit racism, as well as socioeconomic factors—primarily income and educational level—also plays a large role in these inequities.
- There are a number of successful mechanisms for effective cancer prevention and control targeted at underserved African-American communities. These programs demonstrate the importance of linkages between academic practices and grassroots community groups in working together to diminish the social causes of health disparities. One of these mechanisms is community participation in the development, implementation, and evaluation of programs. Directly engaging communities is necessary.
- Materials, including brochures, should be designed with the specific target community in mind. Cultural appropriateness and sensitivity are often overlooked and low literacy levels must be considered, as patients often throw away materials they cannot read or do not understand.
- Program sustainability and longer-term community involvement are very important and should be improved upon. Many grants are for from 3 to 5 years, which is not long enough to sustain relationships with communities. The only way to effect change permanently is through successful long-term community-based partnerships. Sustainability includes not only financial resources, but true community involvement. For instance, Howard University Cancer Center hosts a public health lecture series held in community churches. Also, using other groups and gathering places, such as civic groups, fraternal groups, barbershops and hair salons, makes a difference in reaching the community.

- Overcoming other barriers that impede cancer prevention should also be a priority. Inadequate access to available health care services, competing priorities—including food, shelter, and safety—and basic mistrust of the health care system all contribute to cancer health disparities.
- At Howard University Cancer Center, efforts are made to establish long-term collaborative, community-based partnerships. Social reinforcement strategies, such as the use of lay health providers, community awareness programs, town meetings, and minority investigator training programs, are central to this goal.
- The program development model that provides a continuous loop for assessing needs, clarifying goals and objectives, analyzing internal and external obstacles and resources, and using the data gathered during the feedback phase of the cycle to further inform the continuous process of program development has the advantage of involving representatives from community-based organizations and gaining their commitment to the evaluation process.
- In order to address the lack of minorities in cancer-related professions, it will be important to figure out how to funnel the students coming out of the Historically Black Colleges and Universities that have medical schools, as well as those from the University of Puerto Rico, into the cancer field.

DR. CATHERINE HARVEY

Background

Dr. Harvey currently serves as a Director of the South Carolina Cancer Coalition and Chair of the Board of Directors of the National Coalition for Cancer Survivorship (NCCS). She is a partner in Oncology Associates, a cancer consulting firm that provides a wide range of services to academic medical centers, hospitals, clinical practices, and health care businesses. Previously, she served as Vice President of Clinical Services and Public Policy at OnCare and as Executive Director/Chief Operating Officer of the National Comprehensive Cancer Network (NCCN). Dr. Harvey holds a master's degree in Nursing from the University of North Carolina and a doctoral degree in Public Health from the University of South Carolina.

Key Points

- The cancer community has made great strides in increasing the awareness that cancer care in a clinical trial may be the best treatment option. However, advocacy and educational missions are far from complete. Community-based cancer care is the right venue for the treatment of many people, and it is, in fact, where 80 percent of all adult cancer patients are treated today.
- A patient should not have to forego access to a clinical trial in order to stay close to home. A high-quality cancer clinical trial should, indeed, be the first and best option considered for cancer treatment—not the last resort when all else has failed.
- In order to optimize the outcomes for all people diagnosed with cancer, all patients being evaluated for cancer treatment should know about clinical trial participation at the initiation of therapy; this would help guarantee the best possible evidence base for the treatment. Ensuring that patients are offered a clinical trial will require a commitment from the public, patients, payers, and providers. Public awareness of clinical trials should be strengthened considerably so that patients will demand trial participation. Advocacy groups can help with that effort.
- The current regulatory financing and reimbursement system should be examined to expose the multiple layers of bureaucracy and fragmentation that greatly burden and impede participation in clinical research. Specifically, the new Medicare Prescription Drug, Improvement and Modernization Act (Medicare Modernization Act; MMA) and its impact on office-based clinical oncology, as well as the HIPAA regulations, must be scrutinized.
- The fragmentation and redundancy of the current system of clinical trials review through IRBs should be revised to more efficiently and effectively bring clinical trials to patients. Cancer researchers should be able to concentrate on developing trials and not on the process of getting them approved.

- Community oncology practices that already have high accrual to clinical trials should be identified and studied to evaluate best practices. Communities that have a Community Clinical Oncology Program (CCOP) grant have already begun to address the communication and bureaucratic issues that inhibit clinical research. In communities where there is less organization and more bureaucracy, accrual is handicapped. There is also a concern with MMA that, as the reimbursement process changes, there may be a loss of participation in NIH trials simply because funding will not allow it.
- The accreditation and financial incentives for providers and hospitals need to be strengthened by requiring higher levels of participation, which will expedite answers to important clinical questions. Specifically, programs that require participation by hospitals in clinical trials—such as the American College of Surgeons Approvals Program—could be strengthened. However, if that happens, it should be understood that infrastructure must be paid for independently of the funding for any single trial.
- The collaborations among the NCI, Cooperative Groups, FDA, CMS, academia, the pharmaceutical industry, patient advocacy groups, and others must be examined and revised to maximize participation and involvement in research.
- Best practices in academic hospital and community practices wherein shared decision-making models result in higher accrual to clinical trials need to be identified. NCCS would like to see more time and resources spent on ensuring that patients are always offered a clinical trial and that aggressive palliative care is valued and considered a viable treatment option along with investigations of new curative agents for cancer.
- Until providers are expected to uniformly incorporate high-quality cancer clinical trials as the first and best options for their patients, there will not be a significant change in accrual rates.
- Patients would be much better served if the billing and coding system of reimbursement paid for services patients needed, recognized that research costs money, and was willing to pay for the extra administrative costs and the extra time physicians and research professionals need in order to interact with the patients.

DR. STANTON GERSON

Background

Dr. Gerson is the Director of the Case Comprehensive Cancer Center and the Asa and Patricia Shiverick–Jane Shiverick (Tripp) Professor of Hematological Oncology and Chief of the Division of Hematology/Oncology at University Hospitals of Cleveland and Case Western Reserve University. He is also the Associate Director for Clinical Research at the NCI-designated Case Comprehensive Cancer Center and Founding Director of the Ohio Wright Center for Stem Cell and Regenerative Medicine. Dr. Gerson received his medical degree from Harvard Medical School.

Key Points

- Cleveland lags behind the nation in terms of its high poverty rate, poor educational system, and poor air quality. However, Cleveland's community is committed to biomedical enterprise, with its University Hospitals, Case Western Reserve University, and the Cleveland Clinic. The Case Comprehensive Cancer Center brings those entities together, providing care for over 60 percent of the local population.
- The best cancer care comes from offering clinical trials and clinical research. Education about clinical trials should start at the first office visit, as should prevention education. Also, funding for clinical research conducted by physicians should be encouraged, as should interactions with major medical centers. The cancer community is not doing a good job of evaluating trials, which would greatly help in building trust in the patient community. Patients have no idea which trials are doing well, which ones are not, and which patients are receiving the highest benefits from trials, both specifically and generally. Also, since community oncologists are reimbursed only for drugs that have been approved, they are less able to participate in clinical trials.

- In order to change the practice of medicine in the community, more physicians should be linked to CCOPs, academic medical centers, and NCI-designated Comprehensive Cancer Centers, either financially or through networks. These networks would provide them with up-to-date information about the results of clinical trials and clinical opportunities. Also, it is an important obligation for national funding for Comprehensive Cancer Centers to engage in outreach programs, not only to the patient population, but to the physician population as well.
- Better databases linking clinical outcomes and research should be developed. Databases with patient genetics and samples would allow for a seamless intervention and interaction between the databases that are already available—keeping in mind the complexities of HIPAA regulations.
- Additional funding mechanisms linking component community sites with academic medical centers should be explored. Over 80 percent of patients are cared for in the community; it would be beneficial to link sites together nationally as well as locally.

DR. PAUL SCHAEFER

Background

Dr. Schaefer is Principal Investigator for the Toledo Community Clinical Oncology Program of the National Cancer Institute. He is currently involved in the private practice of medical oncology at the Toledo Clinic. He also serves as Section Head of Oncology/Hematology at the Toledo Hospital; Co-Chairman of the Cancer Committee, Chairman of the Tumor Conference Board, and Clinical Associate Professor at the Medical College of Ohio; and Section Head of Hematology/Oncology at St. Luke's Hospital. Dr. Schaefer received his medical degree from The Ohio State University College of Medicine.

Key Points

- It is fairly easy for community oncologists to get information about clinical trials if they desire to do so. Participating in clinical trials, on the other hand, requires considerable time and effort.
- There are hurdles to getting patients into clinical trials. One is that patients do not know the strength and value of clinical trials, and they are not comfortable with being "guinea pigs," especially if they have just learned their diagnoses and are fearful about treatment. The way to overcome this is education via the popular media; clinical trials need to be well promoted.
- It is becoming very expensive to enroll patients in clinical trials, particularly with the new Medicare guidelines separating reimbursement for drugs from administration of those drugs. If it costs community oncologists to put patients on clinical trials, accrual rates will drop considerably, as reimbursement will not cover the cost of doing business. Also, it takes three times as much provider time—time that is not reimbursed—to put a patient on a clinical trial than it does to administer standard therapy.
- Some insurance companies refuse to enroll patients in clinical trials. This problem should be addressed at the state level.
- Physicians need to be educated about clinical trials beginning in the first year of medical school.
- Patient advocates are an essential part of the entire cancer program.
- The medical oncology community is very up to date on new drugs and therapies and makes an effort to disseminate this information into the community. However, outreach is not universally successful.

DR. K. "VISH" VISWANATH

Background

Dr. Viswanath is an Associate Professor in the Department of Society, Human Development, and Health at the Harvard School of Public Health; an Associate Professor of Medical Oncology at the Center for Community-Based Research at the Dana-Farber Cancer Institute; and Co-Leader of the Health

Communication Core of the Dana-Farber/Harvard Cancer Center (DF/HCC). He received his Ph.D. from the University of Minnesota.

Key Points

- The most effective way to treat cancer is not to get it in the first place. Almost 50 percent of cancers are attributable to lifestyle factors, including smoking and obesity. When talking about translational research, it is important to keep that in mind.
- Research diffusion and dissemination requires an active, systematic, deliberate, rigorous, and tenacious approach. Researchers should put the same emphasis on systematic rigor for translational research as they do on designing laboratory work and trials.
- Systems and people vary in their capacity to learn and use information. Different people and different groups access and use information differently. Not everyone has the same access to information, and not everyone has the same ability to use the information they have.
- Sustainability of interventions is a particular challenge. Researchers must understand scalability of research before embarking on translational research. The certainty of the laboratory evaporates when transferred to the community.
- The focus of translational research should not be just on translation of research and knowledge into practice, but also on the ways in which the community intersects with systems. Different groups come into contact with different systems, including churches, community organizations, hospitals, unions, and Head Start programs. Researchers should ascertain how people intersect with systems and how to exploit those interactions to reach out to individuals.
- Translational research should also actively engage community groups and the private sector to accelerate knowledge transfer.
- There should be incentives for the research community and academic medical centers, including cancer centers, to actively push research dissemination. Pressures, and perhaps even penalties, may also be valuable. Having a coordinator position specifically for diffusion and dissemination and requiring cores in translation may also help institutionalize the process, as well as provide critical incentives and encouragement. Mentoring programs would also help, especially in bringing minority scholars into the system.

DR. STEVEN N. WOLFF

Background

Dr. Wolff is Director of the Clinical Research Education for Career Development program and Principal Investigator of the Minority-Based Community Clinical Oncology Program (MBCCOP) at Meharry Medical College in Nashville, Tennessee. At Meharry, he is a Professor of Medicine, Director of the Sickle Cell Program, and Interim Director of Hematology/Oncology. Dr. Wolff also serves on the Board of Directors and is the Scientific Director of the Lance Armstrong Foundation.

Key Points

- It is feasible to perform clinical research in underserved and poor communities. A third of the patients at the Meharry MBCCOP have no medical insurance, and another third are covered by Medicaid. However, 15 percent of the patients are involved in clinical trials.
- There are practical solutions to the challenge of getting patients into clinical research. First, there must be a mandate for the institution to perform clinical research, with each provider having an incentive, either academic or financial, for having clinical research in his or her practice. There must be an institutional philosophy that clinical research is important to the institution.

- Extra resources are usually required. The Meharry MBCCOP has a U54 grant in partnership with Vanderbilt. This means that there is a shared cadre of personnel and resources to accommodate research.
- Personnel resources must include culturally sensitive and trustworthy people who can talk to patients and earn their trust, assuring them that being put on a clinical trial is a beneficial step in treatment.
- Healthier patients are needed. The number of uninsured patients is increasing, along with poverty and the low health levels associated with it. Too many patients are diagnosed at advanced stages of disease with comorbidities that prevent participation in trials.
- There must be clinical studies that are appropriate to the average patient population. Many study criteria are so strict that average patients do not qualify.
- There are good reasons that patients do not go on clinical trials. Some are simply too sick to participate, either because their disease is too advanced or because they have more comorbidities than are allowable for clinical trial participation. Also, their performance status, which is a measure of general health, is usually worse than that of other applicants.
- General mistrust of the medical community by the African-American community can be overcome if studies are presented in a sensitive and trusting way.

BEST MECHANISMS FOR MOVING RESEARCH INTO COMMUNITIES—DISCUSSION

Key Points

- It is important to strive to establish long-term collaborations between academic sites and their communities.
- There are many medical providers who do not value clinical trials. This needs to be addressed so that more providers see clinical research as an important part of their mission and that trials are perceived as adding value to their practices and benefit the patients coming to see them.
- There is a high cost to doing clinical research, and the need for additional funds and support is real, especially in the community setting. There is also need for IRB oversight and data safety monitoring.
- Providers and researchers should talk to patients and understand their behaviors and lifestyles before recruiting them into clinical trials.
- Putting patients on clinical trials is a burden, and therefore, there must be rewards for doing so.
- Focusing on raising public awareness about clinical trials is extremely dangerous if there is not a trial to offer to every person. There are major problems in the system to fix before public awareness campaigns can begin wholeheartedly.
- A fair amount of evidence has been presented such that, often, the farther one goes away from an academic center and from clinical trials—although the drugs or the treatment might be correct—the greater the likelihood that the dosage and the extent to which therapies are given may not be optimal.

REPORT BACK—DIALOGUE ON KEY BARRIERS AND AVENUES FOR CHANGE: INNOVATION, AFFORDABILITY, AND PRACTICABILITY

INTRODUCTION—DR. LaSALLE D. LEFFALL, JR.

The discussion panel leaders were asked to summarize what was said in their panels and add anything else they would like to express based on their experience and expertise.

DISCUSSION PANEL I: BARRIERS TO TRANSLATING RESEARCH INTO REDUCTIONS IN THE BURDEN OF CANCER—DR. MARK CLANTON

Key Points

- Cancer as a process is little understood by the public. The public understands that there are different kinds of cancers, but few understand that cancer is, in fact, a process that begins at a point of susceptibility. Susceptibility is followed by pre-initiation, the point at which cells begin to change behavior. After pre-initiation comes a malignant transformation of those cells, and in many cases, metastasis to other parts of the body. If the nature of cancer as a process were better understood, the public might think differently about cancer research.
- Most clinical science has focused on the end of the cancer process, when tumors have already formed. However, clinical scientists have become increasingly interested in earlier phases of the cancer process. Trials are being designed that focus on the susceptibility and pre-initiation phases to test cancer prevention and early detection methods.
- Cholesterol levels and other biomarkers are routinely used to screen patients at risk for cardiovascular diseases. In the cancer field, biomarker identification and validation is now beginning to represent a critical component of drug discovery, early detection, and the ability to determine whether therapies are working.
- To improve the understanding of basic scientific questions related to cancer and accelerate drug discovery, the scientific community must improve information sharing among disciplines, especially between the scientific and clinical domains.
- The term *team science* has been used to emphasize the need for improved information sharing. The emerging field of systems biology requires teamwork among a variety of specialists, including physicists, mathematicians, engineers, and molecular biologists. Teams of basic scientists and clinicians are needed to accelerate the translation of new knowledge into new diagnostic tools and therapies.
- Another theme related to information sharing is the importance of translating scientific information into coherent messages to help the public understand the cancer process and assess cancer risk.
- Efforts should be made to increase clinical research focused on early stages in the cancer process to accelerate development of chemopreventive agents and molecular imaging techniques. The regulatory structure that guides the clinical trial process must be reengineered to encourage the creation of trials across the spectrum of the cancer process. Some potentially useful agents and therapies are not investigated because they are not addressed by existing regulations and do not fit existing business models. The current clinical trials system also fails to support bringing together agents developed by different companies.
- The Centers for Medicare and Medicaid Services (CMS) needs increased access to data on the costs of cancer care to allow the agency to make better decisions in the reimbursement process. A dialogue is ongoing among CMS, researchers, and oncologists to address these issues.
- CMS is mandated to pay for off-label use of drugs listed in a compendium published by the Food and Drug Administration (FDA). NCI and CMS are working together to determine how to pay for off-label therapies not listed in an FDA compendium.

DISCUSSION PANEL II: THE ROLE OF ACADEMIC MEDICAL CENTERS IN TRANSLATING RESEARCH INTO CLINICAL PRACTICE—DR. MICHAEL CALIGIURI

Key Points

- The mission of an academic medical center is to translate scientific discoveries into clinical applications and then to scientifically study the outcomes of those applications, providing evidence necessary to implement changes in health care delivery.
- There are insufficient targeted resources to support translational research, and there is a shortage of investigators who are qualified to conduct this kind of research.
- The culture that currently exists in many academic medical centers hinders collaboration between the clinic and the laboratory, favoring departmental versus interdisciplinary programs. There is poor communication among scientists, physicians, administrators, and patients. More emphasis is placed on trying to achieve breakthroughs, which are rare, than on the less glamorous process of making incremental advances.
- Minorities are underrepresented in cancer research performed at academic medical centers, both as investigators and as patients.
- Costs are a serious problem for academic medical centers because third-party payers are reluctant to provide reimbursement for anything other than standard care. If the public and organizations that pay for health care could be sold on the value of translational research, this type of research would be recognized as providing a competitive advantage for academic medical centers in recruiting physicians and patients.
- Potential solutions to these barriers include:
  - Encouraging funding agencies to support grants with multiple principal investigators.
  - Providing supplemental funding for Comprehensive Cancer Centers to support collaborations with academic medical centers.
  - Creating a stable, nurturing environment to ensure rewarding employment in academic medical centers for M.D. and Ph.D. candidates who complete training in an oncology-based discipline.
  - Recruiting minority investigators into M.D. and Ph.D. training programs and clinical fellowships.
  - Removing disincentives, such as wasted time and lost compensation, that too-often occur when physicians in academic medical centers refer patients to clinical trials.
  - Adopting electronic medical records and standardized bioinformatics.
  - Increasing the number of clinical trials focusing on cancer prevention.
  - Increasing incentives for pharmaceutical companies to partner with academic medical centers in conducting treatment trials.
  - Increasing NCI involvement in the drug development process.

DISCUSSION PANEL III: BEST MECHANISMS FOR MOVING RESEARCH INTO COMMUNITIES—DR. ROBERT L. COMIS

Key Points

- The recently passed Medicare Modernization Act will have a great impact on the ability to maintain publicly funded clinical trials. Currently, practitioners are reimbursed for about $2,000 of the costs for each patient, which is from one-third to half of the total cost. On January 1, 2005, there will be an estimated 15 percent reduction in that reimbursement level.
- The advocacy community must remain a strong partner in the effort to maintain and increase the availability and quality of clinical trials and promote awareness of the importance of clinical research.

Examples of progress in this area include recent campaigns by the National Coalition for Cancer Survivorship (NCCS) and Bristol-Myers Squibb's *Tour of Hope*.

- Doctors should be prepared to discuss clinical trials with patients at first contact to provide a consistent message about the benefits of participation. Awareness of the importance of clinical research should be integrated throughout the entire health care system, from academic centers to community-based practices, and doctors must be educated on how to participate in trials.
- Little is being done in an organized way to ensure that therapeutics proven effective through clinical trials are implemented in the delivery of care to the public.
- Bioinformatics is a critical area. The caBIG program should be quickly expanded beyond Cancer Centers to include the whole clinical trials enterprise, including CCOPs and Cooperative Groups.
- Clinical trials should be an integral part of the cancer community's efforts to eliminate cancer-related health disparities.
- To involve communities in joint planning of clinical trials, researchers will have to make the benefits of involvement clear. Those benefits must be sustainable when federally funded research projects come to an end.
- Incentives required to ensure successful participation in clinical research should not be limited to financial compensation. Researchers also need to gain professional recognition for themselves and their practices. Other requirements for successful participation are stable resources and access to adequate numbers of studies to which patients can be referred.
- Mentorship in conducting clinical trials should be provided in medical education.
- It is important to begin educating the public about cancer, research, and trials at a very early age—as early as elementary school.

DISCUSSION

- The public does not understand the language used by scientists, and many scientists do not understand the language used by those working in different disciplines. Government, academia, industry, and other stakeholders must agree to use a common language in addressing the complex problems related to cancer. In addition, medical records and data collected through clinical trials should be stored in a standardized way to ensure their usefulness across geographic borders and among various specialties.
- Incentives for change are needed. This would include encouraging medical students to pursue careers in academic medical centers, residents to pursue academic careers in primary care, and research fellows to remain in academia following their fellowships. Incentives are also needed to encourage physicians to refer patients to clinical trials, encourage industry to engage in prevention and orphan-drug research, and academic medical centers to engage in partnerships.
- The cancer clinical research program in the United States is a delicate medical ecosystem of community-based doctors, academic doctors, patients, and other components. Decisions made about any aspect of this system can have tremendous downstream effects on the research infrastructure in both academia and clinical practice.
- The departmental organization of academic medical centers should be maintained because it fosters rewarding research opportunities. However, the concept of a multidisciplinary research center should be fostered by institutional leadership. Many opportunities for multidisciplinary research are lost because institutions cannot reach a decision on how indirect costs will be allocated.
- Although the status of biomarker development in general continues to be debated, many believe that a biomarker for ovarian cancer may be available soon. This would be a significant advance in addressing a disease that has been very difficult to diagnose.
- In its recommendations following this series of meetings, the Panel should identify actions that can be taken immediately and actions that will require further deliberation and possible legislative action.

Short-term actions could focus on addressing issues related to distribution of direct costs, reimbursement for physicians' time spent on enrolling patients into clinical trials, review of how regulations related to electronic records are implemented, provision of guidelines to industry on endpoints for treatment and prevention studies, and encouragement of ongoing dialogue concerning data sharing.

- The NCI has been replaced by the pharmaceutical industry as the leader in drug development. Barriers to involvement of the private sector in the design of the clinical trials system must be addressed and reduced. Cooperation would benefit the public sector, industry, and academia. Each stakeholder's interests should be acknowledged and addressed; if it appears that only one stakeholder will benefit, partnerships will not succeed.
- Currently, no pharmaceutical companies are making only limited investment in cancer prevention agents. The Federal Government needs to dedicate increased resources to development in this area and deal with the intellectual property issues as they come up.
- Examples of the need to reengineer the clinical trials system include the lack of incentives to address smoking reduction and weight control. There are none because the opportunities for profit do not yet exist.

CLOSING REMARKS—DR. KRIPKE, MR. ARMSTRONG, AND DRS. WILSON AND LEFFALL

- Dr. Kripke identified two issues that the Panel should consider for future discussion. The first is the lack of an appropriate funding mechanism to support clinical trials designed to demonstrate the commercial potential of newly developed agents and therapies. The second is the inherent tension between efforts to reduce the burden of cancer at the population level and efforts to reduce the burden for individual patients and their families.
- Mr. Armstrong noted that language and communication obstacle to collaboration among scientists and other stakeholders, as well as lack of state-of-the-art data systems, present a serious obstacle to progress against cancer.
- Dr. Wilson stressed the importance of helping the public understand the aims of cancer research and the cancer process itself. Important questions regarding efforts to reduce obesity and promote healthy behaviors include determining which generation should be targeted and what institutions or organizations will be responsible.
- Dr. Leffall stressed that discussions about cancer research should not lose their focus on cancer patients. He noted that quality of life is important to cancer patients and survivors. The ultimate goal of translating research into applications is not only to reduce the societal burden of cancer, but also to maintain quality of life.

CERTIFICATION OF MEETING SUMMARY

I certify that this summary of the President's Cancer Panel meeting, *Translating Research to Reduce the Burden of Cancer*, held September 27, 2004, is accurate and complete.

Certified by: LaSalle D. Leffall, Jr. Date: February 16, 2005

LaSalle D. Leffall, Jr., M.D.
Chair
President's Cancer Panel