

**68th Meeting of the National Cancer Institute (NCI)
NCI Council of Research Advocates (NCRA)
National Institutes of Health (NIH)**

Updates on NCI Programs

**Building 31, C Wing, Conference Room 6
NIH Campus
Bethesda, Maryland**

Wednesday, June 10, 2015

Members Present

Mr. Max Wallace, Chair
Dr. Gregory H. Aune
Ms. Mary Ann Battles*
Ms. Susan G. Braun
Mr. William Bro*
Ms. Andrea Stern Ferris
Dr. Sue Friedman*
Ms. Martha Gaines

Dr. June McKoy *
Ms. Kimberly Newman-McCown*
Ms. Heather Ortner*
Dr. Senaida Poole
Mr. Jon Retzlaff
Mr. Roberto Vargas*
Dr. Regina Vidaver

Speakers

Dr. James H. Doroshow, Deputy Director for Clinical and Translational Research, and Director,
Division of Cancer Treatment and Diagnosis, NCI
Ms. Kelley Landy, Acting Director, Office of Advocacy Relations (OAR), Office of the Director,
NCI, and NCRA Executive Secretary
Dr. Paul Pinsky, Acting Chief, Early Detection Research Branch, NCI
Ms. Caryn Steakley, Deputy Clinical Director, Center for Cancer Research (CCR), NCI
Mr. Max Wallace, Chief Executive Officer, Accelerate Brain Cancer Cure, and NCRA Chair

Facilitator

Dr. Clifford Goodman

** Pending Clearance and Appointment*

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Welcoming Remarks and Overview of Agenda

Dr. Goodman, Ms. Landy, Mr. Wallace

- Ms. Landy welcomed participants, noting a number of new potential NCRA members at the table and some outgoing members.
 - Ms. Braun, Ms. Ferris, Mr. Retzlaff, and Mr. Wallace were present and will be leaving the NCRA. Dr. Adam Clark, Ms. Linda House, Mr. Jeffrey Kaufman, and Mr. Josh Sommer were not present; they also will be retiring from the Council after this meeting.
 - New members, pending approval, are Ms. Battles, Mr. Bro, Dr. Friedman, Dr. McKoy, Ms. Newman-McCown, Ms. Ortner, and Mr. Vargas.
- The program featured three presentations:
 - Dr. Doroshov spoke about NCI's Precision Medicine Initiative (PMI) and the Molecular Analysis for Therapy Choice (MATCH) trial.
 - Dr. Pinsky presented data from the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial and the National Lung Screening Trial (NLST).
 - Ms. Steakley, a clinical nurse, discussed the unique work conducted in NCI's intramural program.
- NCRA members introduced themselves and discussed their priorities for research advocacy

NCI Update and Discussion

Dr. Doroshov

- Some of NCI's priorities are precision medicine in prevention and screening, as well as treatment, overcoming cancer health disparities, and basic research that might not have immediate translational implications. There also is a large focus on immunotherapy.
- In addition to translational research, investigators are needed to continue to look at the fundamental processes of metastasis and invasion.
- Health disparities research also is important to NCI as unexplored biologic factors contribute to disparities. The NCI Center to Reduce Cancer Health Disparities supports

training for under-represented minorities and research in cancer health disparities. Studying biological variables with newly available tools is a major goal of NCI moving forward.

- Precision medicine is defined as building a knowledge network for biomedical research and a new taxonomy of disease. In the future, cancers might be named for their genetic characteristics rather than histology or organ site.
- Precision medicine also means tailoring medical treatment to the individual characteristics of each patient, but it also must take a population approach that includes disease prevention and a mechanistic understanding of the causes, pathogenesis, or pathology of disease.
- The President has proposed \$215 million for the PMI: \$130 million to NIH overall with an additional \$70 million to NCI, \$10 million to the Food and Drug Administration to build a database, and \$5 million to the Office of the National Coordinator for Health Information Technology to use electronic health records to incorporate genetic information and address privacy and interoperability.
- In genomic analysis of tumors, researchers are identifying heterogeneity and vulnerabilities in an attempt to try to find common themes and target molecular changes with treatments less toxic than those currently used.
- Responses to targeted therapy can be dramatic and associated with fewer side effects than standard chemotherapy, but drug resistance to the targeted agent is frequent.
- There is a chemical and biological race to develop new tools to hit mutations before they occur.
- The NCI PMI for cancer treatment expands genomics-based clinical and preclinical studies. It establishes genomic master protocol trials of adult and pediatric cancers, a repository of patient-derived preclinical models for evaluating targeted therapeutics, an arm to explore drug resistance, and a national cancer database to integrate genomic information with clinical response and outcome data.
- New patient-derived models for precision oncology to study and overcome drug resistance use several different mouse models that allow researchers to take tumor tissue directly from patients in the operating room and implant them into mice. The mouse models allow testing a large number of tumors from a large number of patients, with propagation that is not possible in humans.
- The adult MATCH trial will open for enrollment in summer 2015. It is the first trial in adult oncology to focus on molecular characterization independent of organ site. The MATCH trial is a public-private partnership with approximately 20 pharmaceutical companies. It will test the effects of a range of targeted treatments on molecular abnormalities in cancers independent of the organ site.
- The MATCH trial will be conducted across 2,400 NCI-supported sites. The initial estimate is that 3,000 patients will be screened to complete 20 phase II trials. Assay findings will be returned to clinicians within 10 to 14 days.

PLCO and NLST Cancer Screening Trials: Data, Image, and Specimen Access

Dr. Pinsky

- The PLCO and NLST data were complex. NCI developed the Cancer Data Access System for public access to the data.
- PLCO, with 154,900 participants, was four trials in one: screening for prostate, lung, colorectal, and ovarian cancers. It compared mortality rates in a screened arm versus a usual-care (control) arm. Eligibility was primarily based on age (55 to 74 years of age). Recruitment began in 1993, with screening until 2006.
- PLCO collected data from a number of questionnaires and several specimens from each participant.
- The only significant reduction in mortality and incidence in the PLCO screening groups was for colorectal cancer.
- NLST, which began in 2000 and enrolled more than 54,000 subjects at 33 centers, grew out of observations in the late 1990s that low-dose CT scans were picking up more cases of lung cancer than chest X-rays. Subjects were randomized to low-dose CT or chest X-ray; there was no control or usual-care group. Each arm had three annual screening rounds and a total follow up of 6 to 7 years.
- The primary NLST outcome was lung cancer–specific mortality; secondary outcomes were all-cause mortality and lung cancer incidence and stage.
- NLST subjects were required to have smoked 30 or more pack-years (where a pack-year equals 365.24 cigarettes), to be current smokers or have quit within 15 years, to be 55 to 74 years of age, not to have had a chest CT within the past 18 months, and not to have a prior lung cancer diagnosis.
- Data collected for NLST were similar to the PLCO information, with more detail on occupational exposure.
- NLST found a 15 to 20 percent reduction in lung cancer mortality in the low-dose CT arm compared to the chest X-ray arm. But low-dose CT has a high false-positive rate of 23 percent and a low positive predictive value of 2 to 5 percent.
- For both PLCO and NLST, access to data and specimens was limited during the active trial phase. As the studies moved to a post-trial phase about 2 years ago, they transitioned to an open access model. Data are available by request, and access to biospecimens is available but requires scientific review.
- To date, 40 datasets and approximately 900 unique variables have been requested from PLCO, and 18 datasets and about 400 unique variables have been requested from NLST. More than half of the PLCO research publications involve biospecimens.
- Some of the research also examines health disparities. A comparison to the National Health Interview Survey demographics indicated that the standard inclusion definition of 30 pack-years might exclude women and minorities disproportionately.

NCI's Intramural Program

Ms. Caryn Steakley

- The mission of the CCR is to engage outstanding researchers in consequential investigator-initiated bench-to-bedside clinical research in a culture of close interaction between basic and clinical science.
- CCR branches focus on preclinical and clinical research related to cancer diagnosis, treatment, and prevention.
- Ms. Steakley reports to Dr. William Dahut, a clinical oncologist who serves as CCR clinical director. Working under her are the director of education and training and the offices of research nursing, data management, protocol support, nurse consultant, and institutional review board administration.
- All patients at the CCR are required to be enrolled in a clinical trial, and every study has a research nurse attached to it. Ms. Steakley has 77 research nurses who work under her.
- Nurses serve as advocates—patient advocates, clinical research advocates, protocol advocates, and participant advocates—in both preclinical and clinical trial phases.
- Patients at the CCR do not pay for their care, and no patients are denied access to a clinical trial because they cannot pay for it.
- Most patients have been ruled eligible for a trial before they get to NCI. The nurses help patients know what will be involved for them. Research nurses are the link between patients and protocols and are responsible for a great deal of detail work.
- Research nurses' roles in coordinating studies include recruiting; screening and scheduling patients, beginning with telephone contact; securing informed consent, including re-consent of some patients; conducting the study; initiating, monitoring, and closing out visits; and coordinating lab pickups and supplies. The research nurses also maintain the integrity of the protocol and regulatory files.
- Patient safety is a primary concern for research nurses. An important responsibility is to report adverse events expeditiously and completely.
- Teaching is another significant component of research nursing. The nurses teach patients and staff, and they mentor other research nurses. Research nurses also abstract, analyze, and publish findings with principal investigators.
- Anyone can come to the CCR if they are eligible for an ongoing trial for their disease. The Clinical Center does not charge patients for participation and treatment in clinical studies at NIH.
- Ongoing trials are listed on the CCR website by investigator or disease.

General Discussion

- Opportunities are needed for partnerships to ensure appropriate representation of racial and ethnic minorities and women in trials. NCI should share lessons learned and broader perspectives about barriers and opportunities for recruitment and retention.
- To engage patients in trials and improve recruitment, the trial outcomes must be important to them. Patients might be interested in more than extending life, and they might not be interested in the same thing investigators are interested in.
- NCRA members are interested in continuing the discussion about minority recruitment to clinical trials at future meetings.
- Advocates could be used to enroll patients in trials more efficiently. A useful topic for an upcoming NCRA meeting might be the infrastructure of recruitment for NCI trials.