NCI to Revamp Clinical Trials; Prompted by Molecular Imaging Advances

The National Cancer Advisory Board (NCAB) of the National Cancer Institute (NCI) announced on June 7 that it had accepted 22 strategic proposals for revamping the NCI cancer clinical trials system and outlined a 5-year implementation plan to accomplish the changes.

Advances in molecular medicine are the driving force behind the Clinical Trials Working Group (CTWG) recommendations. The new blueprint for the NCI's clinical trials enterprise was submitted to the NCAB by the CTWG, a broad-based group convened in 2004 by NCI Director Andrew von Eschenbach, MD. By accepting the report, the NCAB endorsed the CTWG recommendations. "These recommendations propose integrating the best of all components of NCI's clinical trials system into a cross-disciplinary, coordinated research endeavor for moving therapies to patients," said James H. Doroshow, MD, director, NCI Division of Cancer Treatment and Diagnosis, who spearheaded the CTWG. "This new, cooperative enterprise will be supported by a strengthened scientific infrastructure and a broadly engaged coalition of critical stakeholders."

CTWG members representing industry, professional associations, and institutions performing clinical investigations answered questions for NCAB members about the proposals, which were presented in a 77-page report called *Restructuring the National Cancer Clinical Trials Enterprise.* "I greatly admire and appreciate the work of the CTWG," said von Eschenbach. "This report and its implementation plan represent a critical step to reaching the NCI goal of ending the suffering and death due to cancer by 2015. The recommendations lead to creating a clinical research infrastructure that will unravel the molecular mysteries of human cancer and rapidly implement interventions that will preempt the cancer process."

"This enormous potential for more specific cancer treatment, coupled with the complexity of evaluating new, highly specific agents, requires robust clinical trial designs," said Howard Fine, MD, chief, Neuro-Oncology Branch, Center for Cancer Research, who cochaired the CTWG. "Development of such trials will necessitate comprehensive information sharing and close collaboration among clinical researchers and basic and translational scientists as well as scientists developing modern molecular diagnostic and imaging techniques." The report includes an implementation plan with a timeline and budget for each initiative, as well as a recommendation that a formal evaluation system be developed to assess the success of the restructuring effort over time.

The CTWG initiatives are organized into 5 categories. New initiatives propose fundamental and significant changes in the operation of the NCI clinical trials system. Enhancement initiatives propose expansion or enhancement of activities already underway within NCI. The 5 categories are listed here, with new initiatives shown in italics.

Coordination Initiatives

- *Create a comprehensive database containing information on all NCI-funded clinical trials to facilitate better planning and management across clinical trial venues.*
- *Realign NCI and academic incentives to promote collaborative team science.*
- Increase cooperation between NCI, the U.S. Food and Drug Administration (FDA), and industry to enhance the focus and efficiency of oncology drug development.
- Expand awareness of the NCI-FDA expedited approval process to speed trial initiation.
- Work with the Centers for Medicare and Medicaid Services (CMS) to identify clinical studies that address both NCI and CMS objectives, and for which CMS may be able to reimburse some routine and investigational costs.

Prioritization/Scientific Quality Initiatives

- *Create an Investigational Drug Steering Committee to work with NCI to enhance the design and prioritization of early-phase drug development trials.*
- *Create a network of Scientific Steering Committees, which leverage current Intergroup, Cooperative Group, Specialized Programs of Research Excellence (SPORE), and Cancer Center structures, to work with NCI in the design and prioritization of phase III trials to better allocate scarce resources, improve scientific quality, and reduce duplication.*
- *Increase community oncologist and patient advocate involvement in clinical trial design and prioritization to improve the rate of patient accrual and better address practical and quality of life concerns in the design of trials.*
- *Develop a funding and prioritization process to ensure that critical correlative science and quality of life studies can be conducted in a timely manner in association with clinical trials.*

(Continued on page 54N)

imaging support in human patients for the neuroanatomical hypothesis of panic disorder focusing on the amygdala-based fear network."

Neuroreport

PET and Adenomas of the Colon

In an article published in the June 1 issue of the *Journal of Clinical Oncology* (2005;23:3713–3717), van Kouwen et al. from the Radboud University Medical Centre (Nijmegen, The Netherlands) reported on a study designed to determine the utility of ^{18}F-FDG PET in detecting colon adenomas. The study included 100 consecutive patients in whom colon adenomas were suspected on the basis of results from conventional contrast imaging (n = 47) or sigmoidoscopy (n = 53). All patients underwent PET imaging, with positive results defined as focal large bowel tracer accumulation. Colonoscopy was performed after imaging, and histopathologic results from removed adenomas were recorded. Colonoscopy confirmed the presence of adenomas in 68 patients, in 35 of whom PET had identified tracer accumulation at the site of the adenoma. PET sensitivity increased with adenoma size (21% for adenomas 1–5 mm; 47% for those 6–10 mm; and 72% for those larger than 11 mm). PET sensitivity increased with the grade of dysplasia identified at histopathology (33% for low grade; 76% for high grade; and 89% for carcinomas). The overall specificity was 84%. The authors concluded that ^{18}F-FDG PET "detects colonic adenomas and the diagnostic test characteristics improve with size and grade of dysplasia of the adenoma."

Journal of Clinical Oncology

SPECT and Depression After MI

In an article e-published ahead of print in the June 17 issue of *Psychiatry Research*, Schins et al. from the University Hospital Masstricht (The Netherlands) reported on a study using SPECT to assess the pathophysiologic bases of clinical depression in patients after myocardial infarction (MI). They focused on the role of serotonin (5-HT), using SPECT with a ^{123}I-labeled 5-HT(2A) receptor antagonist to study 5-HT(2A) receptor binding. The study included 9 depressed post-MI patients, 10 nondepressed post-MI patients, and 10 healthy control individuals, and results were analyzed using statistical parametric mapping. Depressed post-MI patients showed increased 5-HT(2A) receptor binding compared with nondepressed post-MI patients, and all MI patients showed decreased 5-HT(2A) receptor binding compared with controls. The authors concluded that these data suggest a specific and quantifiable link between seratonin receptor binding and post-MI depression, which in turn suggests avenues of treatment for this frequently noted complication in recovery from cardiac events.

Psychiatry Research

(Continued from page 45N)

- *Develop a standards-setting process for the measurement, analysis, and reporting of biomarker data in association with clinical trials to enhance data comparisons, reduce duplication, and facilitate data submission for regulatory approval.*
- *Investigate integration of phase II trials into the overall prioritization process to further coordinate the national clinical trials system.*

Standardization Initiatives

- *Create, in partnership with the extramural cancer research community, a national cancer clinical trials information technology infrastructure fully interoperable with NCI's cancer Bioinformatics Grid to improve cost effectiveness and comparability of results across trials and sites.*
- *In consultation with industry and FDA, develop standard case report forms incorporating common data elements to improve information sharing among cancer researchers and to optimize data requirements.*
- *Build a credentialing system for investigators and sites recognized by NCI and industry to allow faster trial initiation and keep the investigative community abreast of legal, safety, and regulatory changes.*
- Develop commonly accepted clauses for clinical trial contracts with industry to reduce the lead-time needed to open trials.

Operational Efficiency Initiatives

- *Restructure the phase III funding model to promote rapid patient accrual rates and cost effectiveness.*
- *Reduce institutional barriers to timely trial initiation.*
- Increase patient and public awareness and understanding of clinical trials.
- Increase minority patient access to clinical trials to improve the participation of underserved and underrepresented populations.
- Promote adoption of the NCI Central Institutional Review Board facilitated review process to reduce the time and resources needed to open trials at individual sites.

Enterprise-Wide Initiatives

- *Create a Clinical Trials Oversight Subcommittee of the NCAB to advise the NCI director on conduct of clinical trials across the institute.*
- *Develop a coordinated NCI organizational structure to manage the entire clinical trials enterprise supported by the institute.*

More information about the CTWG can be found at http://integratedtrials.nci.nih.gov. The full report can be found at http://integratedtrials.nci.nih.gov/ict/CTWG_report_June2005.pdf.

National Institutes of Health