Overhaul of NCI Clinical Trial System Still in Progress

By Joanne Nicholas

A decades-long initiative to improve the National Cancer Institute’s Cooperative Group Program has recently made substantial progress. Many credit the April 2010 report from the Institute of Medicine’s (IOM) Consensus Committee as instrumental in focusing NCI on reforms essential to create a clinical trial system to meet the challenges of the 21st century. The report recommended that NCI improve the speed and efficiency of trial design, incorporate innovative science, improve means of prioritization and selection, and offer incentives for participation by adequate support and funding.

The consensus at a recent workshop on the national clinical trial system cosponsored by IOM and the American Society of Clinical Oncology was that NCI had taken the recommendations seriously.

“As a representative from the former cancer cooperative groups, I think it is very important to acknowledge the tremendous and extremely positive impact the involvement of the IOM has had on our enterprises,” said Monica M. Bertagnolli, M.D., of the Dana-Farber Cancer Institute in Boston and chair of the Alliance for Clinical Trials in Oncology. As part of her introduction to the workshop in February 2013, Bertagnolli also recognized NCI’s accomplishments. “Substantial progress has been made in all of these important goals,” she said.

Speaking at the IOM workshop, James H. Doroshow, M.D., NCI deputy director of the Division of Cancer Treatment and Diagnosis, said he thought the restructuring process, started in 1997 or 1998, “is very worthwhile in the degree of change that has occurred.” He predicted that the new National Clinical Trials Network “will make clinical trials more efficient for our patients.”

Doroshow said that NCI has made substantial improvements in restructuring the system, including progress in reducing the time to review and launch a clinical trial, standardizing agreements with industry, developing a core facility to support imaging and radiation therapy trials, and strategic planning and trial prioritization at the national level. He seemed proudest of NCI’s new uniform clinical trial data-management system, which operates across more than 3,000 trial sites. “There is no country, there is no pharmaceutical organization that has a way to enroll patients 24/7 like we have,” said Doroshow.

In a phone interview, Sheila Prindiville, M.D., M.P.H., director of NCI’s Coordinating Center for Clinical Trials, pointed to NCI’s June 2012 release of six Requests for Applications for the new clinical trial system as “a major accomplishment” in setting national clinical trial priorities. The applications will be reviewed this year, with funding awards issued in March 2014.

Two ongoing changes that should increase efficiency and help with clinical trial accrual are a streamlined patient consent form and a centralized institutional review board (IRB). In December 2012, the Association for the Accreditation of Human Research Protection Programs awarded NCI’s centralized IRB full accreditation, and it is now the NCI’s IRB of record. “We believe this will simplify things for centers to participate and remove what may have been a barrier,” said Prindiville.

Several working groups had tackled revising patient informed-consent forms. “Over time, we found the lengths of informed-consent forms had grown—some even to 35 pages—and seemed like a legal document,” explained Prindiville. “A goal of the IOM was to update NCI’s consent document to be different for each trial but with a standard template, kept to a bare minimum in length while transmitting the central information of risks and benefits to patients,” she said. “We hope the streamlined conveyance will help with accrual for clinical trials by making it less burdensome for physicians and patients.”

Many of the changes have been well received. “I think the thing the NCI has done well is generate a list of things they want to do, and through James Doroshow and Sheila Prindiville’s leadership, they have done it,” said James L. Abbruzzese, M.D., of the University of Texas M. D. Anderson Cancer Center in Houston and chair of NCI’s Clinical Trials and Translational Research Advisory Committee. Though he praises their accomplishments, he thinks it is too soon to know the effects: “I think in 5 or 10 years we’ll see whether the trials have a positive impact.”

Five New National Cooperative Groups

To strengthen the cooperative groups and streamline operations, NCI downsized the nine adult cooperative groups and one pediatric to four adult groups and the Children’s Oncology Group. “Is this iteration the best

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Immunotherapy To Treat Leukemia Possibly Ineffective for Advanced Disease

By Gunjan Sinha

Immunotherapy presents a promising approach for blood cancers resistant to treatment, but it may be effective only in patients with minimal residual disease. In a mouse model of chronic myeloid leukemia (CML), researchers at the University of Bern, in Switzerland, showed that adoptive transfer of cytotoxic T lymphocytes (CTLs) reduced numbers of leukemia stem cells (LSCs) when leukemia antigen levels were low. Paradoxically, in mice with more advanced disease, transferred CTLs induced LSCs to proliferate and caused the cancer to progress more quickly. Moreover, the study for the first time implicates gamma interferon (IFN-γ), a major cytokine that CTLs secrete, as a major player responsible for this dual behavior of CTLs.

The findings “have high translational relevance,” said Martin Bornhäuser M.D., at the Carl Gustav Carus University Hospital.