LETTER FROM THE EDITOR

The Institute of Medicine (IOM) is a not-for-profit, nongovernmental agency that is one of the United States National Academies, which also include the National Academy of Sciences, the National Academy of Engineering, and the National Research Council. The designated role of the IOM is to provide unbiased advice on issues related to biomedical science, medicine, and health. Its ranks are filled by leaders in various disciplines whose objective is to improve the health of the nation. Thus, when the IOM issues a report, everyone takes notice.

And notice was taken recently with the report released on April 15, 2010 on the clinical trials situation in the United States. I received several e-mails from ASCO, CALGB, and the Lymphoma Research Foundation, and read articles in such sources as *The New York Times*, which ran an editorial on April 24. The particular focus of the IOM report was on "revitalization" of the National Cancer Institute's (NCI) Clinical Trials Cooperative Group Program. These cooperative groups have been in existence for more than 50 years and have conducted the highest caliber of clinical trials, resulting in new drug approvals, changes in patterns of care, prolonged patient survival, and major scientific observations. At one time, there were more than 20 groups sponsored by the NCI; the current number has been whittled down to 10, including 14,000 investigators at 3,100 institutions, who accrue more than 25,000 patients per year.

Whereas pharmaceutical-sponsored trials get new drugs to market, the cooperative groups perform trials the companies have little interest in: studies in rare diseases, novel combinations, how to optimize doses and schedules of drugs already on the market, multimodality strategies, and correlative science and psychosocial issues.

In general, the 17-member IOM panel was supportive of a cooperative group system. The IOM report recognized the contributions of the groups, but criticized them as being slow and cumbersome, with a third of trials closed before completion. Specifically, the IOM proposed ways of improving the design, review, and conduct of trials. One approach would be to reduce the time from the generation of an idea to its approval, which is currently about 2.5 years, by which time the idea is often outdated and irrelevant. Amongst the recent attempts to facilitate the process are the NCI-coordinated, disease-specific steering committees, comprised of members of the cooperative groups, cancer centers, and Specialized Programs of Research Excellence (SPOREs), as well as patient advocates and other stakeholders. These committees were created to prioritize studies, particularly phase III and large phase II trials. Strict timelines have been implemented such that studies not activated within a predesignated time frame will be terminated.

The IOM set a goal for the creation of biorepositories, with the cooperative groups assuming the caretaker role because of their extensive experience. The IOM panel also encouraged the development of novel trial designs to help speed up conduct of the studies and to increase patient accrual and diversity. Importantly, they supported an increase in the amount of funding and support for clinical investigators and coverage of patient care costs in clinical trials. They encouraged more public-private partnerships and hybrid funding mechanisms whereby the government and industry can partner on supporting trials.

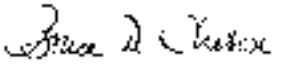
On the other hand, a major recommendation was to decrease the number of groups and committees, to the point of creating multidisciplinary, disease-specific groups. Having been in this business for decades, I remember that there were a number of disease-specific groups: the Lung Cancer Study Group, Brain Tumor Study Group, Wilms Tumor Study Group, Leukemia Intergroup, GI Tumor Study Group, and others. That experiment failed, and most of these groups are but a faded memory. (Although two still in existence—the Gynecologic Oncology Group and the National Surgical Adjuvant Breast and Bowel Project—have done rather well for themselves.)

The infrastructure for collaborative trials would be consolidated, in an attempt to make the system more streamlined and consistent. Who would decide which operations systems and statistical strategies are best for all? The NCI's role would shift from oversight to a focus on supporting high-priority trials. It is hoped that this change would facilitate, rather than impede, clinical research. Other goals included prioritizing ideas and sites, increasing participation by both patients and physicians, increasing the use of biomarkers, defining standards for minimal data requirements to establish safety and efficacy, reducing costs, and increasing collaboration amongst the various participating parties.

Although many of the IOM recommendations sound reasonable, there is a huge potential downside: the possibility of impeding innovation and slowing accrual. For example, a group may be coerced into activating a phase III trial when innovative pilot studies might be more appropriate. Groups also succeed because their members have a sense of partnership: a veritable team spirit. Participants, especially from the community, care for patients with a variety of cancers and would thus be faced with participating in multiple site-specific groups.

Clearly there is a need for further discussion. Despite underfunding and overregulation, the cooperative groups have set the standard for quality clinical trials for decades. It is hoped that representatives from the groups will be given the opportunity to participate in the revitalization process, or else interest in large collaborative trials in the United States may fade, taking the goal of curing cancer with it.

Until next month . . .



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