Site Qualification in Multicenter Clinical Trials

We are facing a potential paradigm shift, moving from the traditional gauge of drug efficacy based on tumor shrinkage, which can take months to manifest on a CT scan, to a biomarker-based system that can detect a therapeutic response within days. Under the new paradigm, we will examine the biological characteristics of each tumor to understand and predict its response to therapy; this will lead to reduced costs, faster drug development, and improved therapeutic efficacy.

Molecular imaging's potential to facilitate the cumbersome and expensive process of drug development is acknowledged by both the pharmaceutical community and the U.S. Food and Drug Administration (FDA). However, a lack of standardization across platforms and imaging centers has been a major obstacle to the use of molecular imaging biomarkers as endpoints for clinical trials.

This critical need for standardization of methodology also has been widely acknowledged by the imaging community. A report from the American College of Radiology Imaging Network in the July issue of *The Journal of Nuclear Medicine* (2009:50:1187–1193) enumerated a number of the issues that contract research organizations (CROs) and the therapeutic development community have been asking the molecular imaging community to address.

A major goal of the SNM Clinical Trials Network is to address this need and, in the process, develop a critical bridge between therapeutic developers and the imaging community. We are building a network of qualified imaging centers that will be able to provide data to meet the regulatory burden of proof demanded by the FDA. We are developing tools to standardize data acquisition and to train imaging personnel in standardized imaging protocols, good clinical practice (GCP) standards, and image interpretation. We are also sponsoring a series of workshops to bring the drug development, regulatory, and imaging communities together so that all parties will be clear on expectations and on what the imaging community can deliver.

As part of this dialog, on June 13 at the SNM annual meeting in Toronto, Canada, the network sponsored a day-long workshop highlighting the continuing need for standardization of imaging sites involved in multicenter clinical trials. Speaking at the workshop, Bernard Fine, MD, PhD, from Genentech, noted that the high rates of failure at every stage of the clinical trials process point to a critical need to improve evaluation procedures in early-stage drug evaluation, with the goal of reducing the number of pivotal phase 3 trials that fail. In terms of cost savings, even a moderate decrease in the failure rate would be significant. He described pharmaceutical companies' needs for a mechanism that provides a broad choice of clinical sites, shortened time for initiating clinical studies, and confidence in the quality/consistency of imaging data from multiple clinical sites. The ability to accumulate data from multiple sites is critical to this effort, because it helps ensure adequate numbers of patients in an acceptable time frame, which leads to faster impact on clinical practice.

At the same workshop, Wendy Hayes, DO, from Bristol-Myers Squibb, outlined the difficulties pharmaceutical companies have encountered in obtaining useable results from multicenter imaging studies. She addressed the need for improving routine quality assurance across multiple sites through training and the use of a standardized phantom program as well as a need for improved awareness of the importance of complying with standardized imaging procedures.

SNM's Clinical Trials Network was conceived to provide the therapeutic development community with assurance that the imaging data from SNM-qualified sites would be of the highest quality and quantitative integrity. We are currently registering potential imaging sites, assessing their current capabilities, and developing programs to help sites qualify for participation in the network.

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