Clinical Trial Development of Nonproprietary Imaging Agents

It has been 15 y since the introduction of a new "successful" nuclear imaging agent. Despite the existence of many well-known tracers in the literature (e.g., ^{18}F-FLT, ^{18}F-MISO, ^{18}F-DOPA) and years of work under individual site investigational new drug (IND) mechanisms, FDA approval for widespread use of these agents is no closer than when they were first introduced. As an imaging community we have failed to define pathways to identify and validate the clinical role of promising radiotracers like these—until now.

Over the past few months, the SNM leadership has carefully reviewed the barriers and bottlenecks preventing radiopharmaceuticals from gaining regulatory approval and clinical acceptance. Although each agent has its own complex challenges, the chief common roadblock is the absence of an *affordable* framework to facilitate the approval process for public domain, nonproprietary agents. Specifically, an approved pathway at the regulatory level is needed to help investigators collect adequate and acceptable multicenter clinical trial data.

In response to this challenge, in September of this year SNM launched an innovative process for integrating imaging biomarkers into phase 1, 2, and 3 clinical trials of new pharmaceuticals, leading to a pathway for the regulatory approval of both the pharmaceutical and the radiolabeled probe as an imaging biomarker. The plan has led to the creation of the Molecular Imaging Clinical Trials Network.

The Clinical Trials Network is a program that reaches across the domains of pharmaceutical development, imaging, radiopharmaceutical manufacturing, and regulatory agencies to integrate the use of investigational imaging biomarkers into multicenter clinical trials that are being planned for investigational therapeutics by the pharmaceutical industry. These therapeutic drug development trials can serve as vehicles for nonproprietary imaging biomarkers that need a creative answer to the demands of expensive clinical trials. Simultaneously, the drug development time can be reduced, so both imaging and pharmaceutical development benefit.

The network will provide SNM-sponsored centralized INDs for biomarkers of interest and will coordinate standardized imaging protocols across qualified multicenter clinical trial sites. The network will work closely with the FDA to ensure proper definition of imaging and manufacturing protocols for biomarkers with INDs approved through the network. Working with the FDA to design the clinical trials will ensure that biomarker data from these studies will be acceptable for consideration of a new drug application.

According to the FDA, in the past the agency has struggled with inconsistent imaging methods at different centers, making it very difficult to assess results in multicenter trials. To address this, the network plan includes the creation of a registry of imaging centers that demonstrate a willingness and ability to adhere to standardized methods. Sites in the registry will participate in a PET phantom program that will help all registered imaging sites to demonstrate adequate current standard imaging capabilities and staff training as well as the ability to adhere to standardized methods. Enrollment in the registry has already begun, with more than 100 sites currently identified.

The network received FDA approval for the first centralized IND in September. The IND application is for ^{18}F-FLT, an investigational PET imaging biomarker with apparent promise for demonstration of tumor proliferation. Several pharmaceutical developers have already expressed interest in utilizing this approved IND in near-term clinical trial work. Active clinical trials utilizing FLT are expected to begin in 2009. Once ^{18}F-FLT is in clinical trial using this first centralized IND, we will begin developing the next generation of INDs.

SNM is planning ongoing educational sessions in multiple formats to help the imaging community better understand the roles and responsibilities of participation in the registry, the phantom program, and multicenter clinical trials. The Molecular Imaging Clinical Trials Network will be launched at a special workshop scheduled for February 8 and 9, 2009, in Clearwater, FL, immediately following the SNM Mid-Winter Educational Symposium. The workshop will provide detailed information on the network, train attendees on the roles and responsibilities of participation in multicenter clinical trials, and discuss the specific imaging and manufacturing protocols contained in the ^{18}F-FLT IND. We are strongly encouraging attendance at this workshop for anyone—pharmaceutical company representative or imager—who has an interest in a multicenter study that combines an imaging biomarker with a therapeutic drug clinical trial.

We are confident this program will be successful, because we are finally removing the bottlenecks that have existed for both drug developers and imagers over the last 15 y (or more), and we are doing it with the cooperation of the FDA. The FDA, pharmaceutical companies, and the SNM community have all been extremely cooperative in designing the Molecular Imaging Clinical Trials Network because it is about building bridges and moving the field forward.

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