BY DENISE MYSHKO

PHASE I: Patient Recruitment

Recruitment challenges begin in Phase I and include targeting, positioning, and communicating the value of clinical trials to study sites and patients.

According to Peter Smith, Ph.D., senior VP, nonclinical development sciences at Millennium Pharmaceuticals: The Takeda Oncology Company, shortages in funding, manpower, and patient availability have created the proverbial perfect storm in the current clinical trial system.

"The fact that traditional clinical trial endpoints in assessing novel agents are being reconsidered only puts more pressure on an already strained system," he says.

Jerome Bailey, VP, early phase business center, at Omnicare Clinical Research, says the number of inclusion/exclusion criteria has almost doubled in an effort to recruit the ideal subject.

"Sponsors are increasing their overall screening of CRO and clinical pharmacology units (CPUs) with expectations to ensure rapid patient/subject enrollment and that the data collection methods allow faster turnaround to provide answers on safety earlier," he says. "Studies that typically exposed subjects are now moving to patient populations. Additionally, fewer patients/subjects are willing to participate because of these factors, and the screen fail rate has increased, leaving many CPUs requiring a higher advertisement budget to procure the ideal patient/subject. All the while, the sponsors' desire to decrease cost has caused a strain on the overall network and willingness of CPUs to take on the work that may not provide adequate margins for work performed."

Jamie Dananberg, M.D., executive director of clinical pharmacology at Eli Lilly and Company, says an increasing number of studies seek to enroll patients to assess certain pharmacologic signals that can only be detected in the disease state.

"These patient studies present a number of challenges that are unique," he says. "Furthermore, there will naturally be limitations in the availability of patients, particularly in certain disease states, as the quantity of early-phase or translational clinical research in patients increases from both industry- and academia-sponsored studies."

Brian Sanderson, M.D., medical director, Chiltern Early Phase, says patients are increasingly being entered "first line" into Phase I studies as part of the drive to get early proof of concept.

DR. ALAN COPA ■ *Cetero Research*

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"These studies by their very nature are nontherapeutic, thus the patient will not benefit immediately nor directly from taking part in the study, unlike patients enrolled into later-phase studies," he says. "They also tend to be placebo-controlled studies, which can be an issue for participation. Such studies are usually very intensive and can take up a lot of a patient's time, more so than later-phase trials. In addition, there tend to be more restrictions for patients in nontherapeutic trials; i.e. the length of time the resident is in the clinic, restrictions on food, drink, alcohol consumption, etc. All of these factors — as well as the fear factor of taking an experimental drug — may inhibit patients from taking part in trials. There also may be resistance by healthcare plans to include their patients in nontherapeutic studies because of the nature of the trial."

Dr. Bailey says meeting patient/subject recruitment goals has become harder because aggressive timelines have been set.

DR. BRIAN SANDERSON ■ *Chiltern*

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"There is little to no room for delays or postponements for protocol rewrites, drug delays, or other changes," he says. "Any potential problem with getting the study started especially when subjects/patients recruitment strategy/plan has been developed and site selection has occurred can similarly have a negative effect on recruitment. With the number of study-related activities and PK draws increasing, subjects are less likely to want to participate in these trials because of their time-consuming nature. For patients, the desire to participate in a study that furthers the scientific knowledge of their disease or the potential to promote a product that

may help them has also created a challenge for recruitment. Patients have become more selective and often seek out the trial that furthers their cause."

Patient/subject recruiting is the one challenge in particular that must be proactively managed, Mr. Bailey says.

"The overall site selection process must include a method to ensure that sites have three to four times the normal recruitment expectations and have a savvy recruitment staff," he says. "The standard newspaper ads or flyers are no longer working."

A key to recruitment is having a strong patient database from which to recruit, says Alan Copa, Pharm.D., president of clinical operations for Cetero Research. Having proactive strategies in place to ensure that recruitment databases are well-maintained is imperative.

"CROs that are the most successful in their recruiting efforts proactively implement recruitment strategies to constantly build and clean their database," he says. "In addition, it is essential that as much of the data be collected electronically to deliver a clear data set as quickly as possible when the clinical conduct of the study is complete. Proper protocols, processes, and standard operating procedures are the foundation of successful studies. Training associates to understand and adhere to the protocols improves efficiency and quality."

And in this electronic media age, pharmaceutical companies should consider using Facebook, MySpace, and Twitter to attract the attention of the potential patient/subject, Mr. Bailey adds.

"IRBs must be more willing to allow these new media along with other unconventional methods," he says. "Using these electronic social sites has become more acceptable to make contact with patients and subjects. In this electronic age, subjects, but moreso patients, are willing to travel greater distances to be exposed to new treatment possibilities. The location of the patient should be secondary, especially as the Phase I study becomes associated with a Phase IIa trial." ✦