

BY ROBIN ROBINSON

→ PHASE III TRIALS: Patient Recruitment and Data Collection

Technology solutions that improve patient recruitment and data collection and management may be just what the industry needs to reduce costs and improve efficiency.

FAST FACT

AT LEAST 80% OF TRIALS EXPERIENCE A DELAY OF AT LEAST A MONTH BECAUSE OF PROBLEMS RECRUITING CLINICAL TRIAL PATIENTS.

Source: CBR Pharma Insights

Two of the biggest bottlenecks in the drug development process, particularly at the Phase III juncture, are patient recruitment and data management. Experts say technology, partnering, and strategic planning can improve Phase III clinical trial efficiency.

Phase III: Recruitment Technologies

According to industry sources, almost 70% of U.S. trials do not enroll patients on time, but with better planning trials are more likely to be delivered on time and on budget. Technology advancements and increasing patient empowerment can help expand the opportunity to reach more patients who may be interested in participating in a clinical trial.

Phase III clinical trials are all about driving site performance, recruitment, retention, consistency, and quality, says Nigel Hughes, founder and director of Firecrest Clinical.

“Despite all of the technological advances in the running of Phase III clinical trials, the industry is still challenged with one interesting statistic: on average, in any given trial, about 30% of investigative sites recruit 70% of the patients,” he says.

The issues of patient recruitment, protocol deviations, and the need to continually review and clean data routinely add to the spiraling costs of clinical trials today.

“For sites conducting many clinical trials, the challenge facing investigators is determining the suitability of patients for recruitment to any one of those studies,” Mr. Hughes says.

Traditionally, the industry has responded



NIGEL HUGHES ■ Firecrest Clinical

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with elaborate investigator meetings and a heavy focus on training. It is estimated that more than \$2 billion is spent annually on such meetings with little or no demonstrable benefit in improved site performance.

According to Mr. Hughes, there are new ways to drive investigator site performance using simple communication tools delivered via the Internet, coupled with protocol specific virtual training methods that can be tracked by the sponsor down to site and user level.

“Early studies using these tools and techniques have shown effectiveness in increasing patient recruitment and producing cleaner data — ultimately reducing costs,” he says.

According to Martha Feller, Ph.D., global executive VP of operations at i3 Research, to

JOHN BENBROOK ■ MMG

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improve patient recruitment, sponsors and CROs should apply the concept of “thinking globally, acting locally:” in other words, set strategy and project milestones at the global level, but use local know-how and implementation to drive successful patient recruitment.

With almost 80% of U.S. trials failing to enroll patients on time, sponsors should seek robust informatics capabilities, including a feasibility assessment tool that will identify unrealistic protocol criteria, as well as plan more sites when patient counts are forecast to be low.

“Feasibility studies, including quantitative and qualitative analysis from each region involved, should be started early to finalize the protocol and support the country selection,” Dr. Feller says. “When possible, available quantitative data on treatment patterns, patient prevalence, concomitant, and co-morbidities should be used.”

Sponsors must also match design protocols with regulatory agency requirements, says Stuart Young, executive VP of clinical monitoring at Chiltern. This may result in challenging protocol inclusion and exclusion criteria that

can limit the potential patient population available to the study.

"To maximize the chance of reaching recruitment levels, it is imperative to concentrate a great amount of energy on study start-up," he advises. "Having solid regulatory intelligence regarding which countries to choose or drop is the first step. Performing detailed feasibility studies to optimize country and investigator selection is key. This can be achieved by using proprietary databases as a first pass, then moving on to sponsor or CRO databases, and using prior investigator performance pertaining to achievement of patient recruitment versus the target."

Ensuring patient recruitment rates are realistic through more data-oriented planning and objective feasibility analysis can also improve site performance, says Stephen Cutler, Ph.D., senior VP and chief operating officer at Kendle.

"This analysis, coupled with better up-front planning, will enable trials to be delivered on time and on budget," he says. "By understanding what has actually been achieved on previous trials, enrollment plans and projections can be prepared with a much greater degree of accuracy. We also need to better understand where the patients are, who is treating them, how they get to the sites and into the trial, and how to proactively reach them."

The time has come for comprehensive, end-to-end recruitment strategies that are forward-thinking from protocol feasibility to retention, says John Benbrook, CEO of MMG.

"Recruitment planning needs to begin with the protocol feasibility assessment through the collection of data from as many sources as possible, including population, prescription, and diagnosis data, as well as clinical trial intelligence," he says. "The rigorous application of advanced analytics to this data set also drives site selection, which in turn informs the recruitment strategy. In-depth analysis is needed prelaunch for a holistic strategy for recruitment and retention to be orchestrated. Early alignment of recruitment strategies is the key."

James DeSanti, founder and CEO of PharmaVigilant, says with resources becoming more scarce, sponsors should look to technology to improve recruitment and enrollment.

"Sites that are using comprehensive technology suites that address multiple facets of a trial, beyond simple data collection, are better equipped to focus on recruitment and enrollment issues," he says. "Sponsors should also look for technology that is patient-based rather than technology that is linked to the site. This ensures that patients who may change their location during the trial — for example, move to Florida for the winter or are seen by more than one physician, or participate in a pregnan-



DAVE EVANS ■ Octagon
Research Solutions

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cy registry, or are involved in more than one study, or are involved in studies that extend over several years — do not have to be re-entered or drop out of the trial altogether. In addition, identity protection and privacy are necessary to ensure the safety and security of a trial participant's personal information. Any patient-based technology should guarantee that sponsors cannot view or access patient information."

The increasing size and geographical spread of clinical trials require the implementation of electronic technologies to meet data monitoring requirements and concise timelines, says Nagaraja Srivatsan, VP and head of life sciences, North America, Cognizant.

"Integration of data from the widely distributed sites across the globe and the integration of the various data collection technologies being used at different stages of clinical development for one data repository are key to successful enrollment," he says.

According to Sean Smith, VP of logistics and Asia at Fisher Clinical Services, a movement toward more collaboration and communication between stakeholders is a major paradigm shift.

"In the last five to 10 years, companies have met the patient numbers for Phase III trials by opening more sites in more countries," he says. "There is now a realization that this strategy is unsustainable and very expensive. Less than 30% of sites do not recruit enough patients to meet requirements, increasing the coverage on clinical materials, incurring high CRA costs, and adding to overall study timelines."

In the next 10 years, Mr. Smith predicts companies will turn their focus to high-volume/high-delivery sites in all regions, including the United States, European Union, Asia, and Latin America.

"This strategy will require GCP providers to make better use of technology to provide sites with 24/7 help desks to remove the dependence on the CRA, and GMP services — inventory, storage, accountability, and returns management — have to be increased for sites," he says.

Phase III: Data Technologies

Advances in technology and automation allow clinical development teams to spend

INVESTIGATOR PAYMENTS

A recent study by Cutting Edge Information shows that during Phase IIIb development companies budget an average of \$32,513 for principal investigator compensation. Yet investigators receive an average of only \$13,436 for a Phase IIIb study, 59% less than budgeted.

The significant differences between these amounts — what's budgeted and what's received — emphasize cost-saving opportunities for drug and device manufacturers. Benchmarks validate the notion that sponsors have more negotiating room with CROs and other sites than they may have previously believed.

The biggest concern in investigator compensation, however, may be mounting public scrutiny. Drug companies are already facing a public relations scenario in which payments to physicians for promotional or educational activities have come under frequent fire.

Still, oversight may be inevitable. In an environment of ever-tightening regulation and oversight, companies need to be proactive in employing processes seeking to protect them against future regulatory scrutiny. This situation presents companies with an entirely new set of challenges.

For example, relationships between investigators and companies can take many forms, including contact through investigator-initiated trials, CROs, and academic institutions. Trying to address these nuances is a challenge. To protect themselves, companies are considering a fair-market value approach to investigator compensation.

Source: Cutting Edge Information.
For more information, visit cuttingedgeinfo.com.

more time on higher-value activities and extend experienced resources.

"Lean methodologies that have been successfully applied in other areas, such as manufacturing, are being adopted in development to streamline processes and increase quality and consistency," says Barbara Tardiff, M.D., corporate VP at Parexel International. "A substantive change in thinking within organizations often must occur to realize the advantages and benefits of these emerging opportunities. Cost and time savings can be achieved through innovation that promotes automation, streamlined processes, standardization, and improved alignment and consolidation of resources."

In the transition from early-stage studies to



DR. STEPHEN CUTLER ■ *Kendle*

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later development, the ability to scale efficiently becomes critically important.

"Technology can also be used to streamline workflow as a growing convergence between systems and the improvement in integration technologies enable diverse applications to work synergistically," Dr. Tardiff says. "For example, information from EDC, safety/adverse event reporting, and clinical trial management systems can be used to systematically direct the frequency and content of monitoring visits, providing a more purpose- and data-driven approach, and allow monitoring resources to be applied where they have the greatest impact on enrollment, data quality, and regulatory compliance."

Global pharmaceutical and biotech companies continue to struggle with the complexity of managing clinical information throughout the clinical information life cycle. Technology adoption allows the highly complex process of data exchange in clinical research to operate at optimal performance and speed, experts say.

"It's especially important now, when there are new sets of offerings, that sponsor companies or CROs access the most state-of-the-art technology without having to build up an expensive infrastructure in-house," says Patricia Bassett, VP sales EMEA, Unithink. "The new SaaS (software as a service) model signifies an important opportunity to reduce the time and cost of setting up clinical trials."

There is no reason for companies to not fully use technology for every aspect of their trials, she says.

"The earlier barriers, such as cost and technological readiness, have been removed," Ms. Bassett says. "When I hear of a company that is not using technology, my first question is 'Why not?'"

As companies continue to expand into emerging regions and conduct global trials, the need for a data warehouse to streamline the decision-making process and allow faster trial close out is essential, Mr. DeSanti says.

"Data warehouses are key to the data collection, monitoring, and reporting process; warehouses provide greater access and control of clinical trial data and offer more flexibility and customized options in terms of reporting," he says. "Data warehouses ensure the right information is given to the right person at the right time."

Another technology solution that is a key factor in Phase III trials is remote monitoring, which provides ongoing data monitoring independent of site visits, resulting in significant time and cost savings.

"Monitoring is often one of the most expensive and time-consuming line items during the Phase III process, but a remote monitoring solution ensures that delays and extra expenses are avoided," Mr. DeSanti says.

Overall, however, sponsors should be looking at technologies that offer the highest quality solution available.

"Innovation is key, but if the technology solution doesn't provide accurate, actionable information then trial efficiencies cannot be realized," Mr. DeSanti says.

The industry must be able to solve the fundamental issue of exchanging information, both data and metadata, in a way that allows for efficient machine-to-machine interoperability, says Dave Evans, chief information officer of Octagon Research Solutions.

"The use of individual technology solutions to address a functional point requirement compounds the issue of data interchange enormously," he says. "Identifying the individual technology solutions that are key to ensuring efficient Phase III trials for a functional segment would be not addressing the puzzle of efficiency as a whole."

Mr. Evans suggests that an enterprisewide metadata registry (MDR) is paramount for the success of any efficiency-driven process and organization. Mature organizations are now being challenged to manage the resulting chaos of integrating point technology solutions without a stable, enterprisewide clinical information standards strategy in place and active.

"Most organizations don't have a standard way to describe how data are collected and transformed over time," he says. "They have no mechanism for managing and communicating metadata standards. There is no governance process and no global standard to con-

vey. As a result, many study teams reinvent the wheel with each new study."

According to Mr. Evans, the information exchange between partners is burdened by the friction of data conversion from one format to another. The knowledge of the data context is not carried forward from one functional area to another area, especially between an external organization and a sponsor. The data lineage information is often nonexistent and is extremely difficult to re-create retrospectively.

"For these reasons and more, it is imperative that an organization move decisively toward the implementation of a metadata registry to handle the standards and processes that govern the way information is designed, collected, processed, analyzed, reported, and interchanged," he says.

Of all the clinical technology solutions being used today, one that has proven to enhance productivity is the integration of data and information from the use of data-driven study portals, says James Esinhart, Ph.D., executive VP of global biometrics and North America business unit at Chiltern.

"The array of clinical technologies used for a clinical trial are most often disjointed systems, and while there is nothing wrong with that approach, developing data driven study portals with simultaneous access to these disjointed systems truly empowers researchers to best monitor and manage a large global program," he says.

Dr. Esinhart says this is an area that the clinical technologies industry cannot ignore.

"Rather, companies should be looking forward to conquering this next milestone to improve quality, efficiency, and overall patient welfare in clinical trials," he says.

By enabling the core functionality of one solution to be accessed from another, this convergence of solutions is a dramatic shift in the way that technologies can be used together to streamline workflow while facilitating more effective trial management, says Steve Kent, president of Perceptive Informatics.

"In the past, clinical data were simply moved between applications to reduce the need to reconcile independent databases," he says. "The new level of integration, which must be scalable, is focused on simplifying processes to create highly optimized experiences for users." ♦

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