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Rethinking Patient And Site Engagement

Thought Leadership In Association With ICON

by

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Drug development costs are increasing annually, with clinical trials identified as one of the most expensive and time-consuming stages of the development process[1]. One factor contributing to this cost inflation is more complex study protocols, which can lengthen trial times while increasing the burden on sites and patients.

Growing complexity is increasingly pervasive. Between 2001-2005 and 2011-2015, the number of endpoints in pivotal Phase III clinical trials almost doubled from seven to 13, according to the Tufts Center[2]. Over the same period, there was also a 70% increase in the total number of procedures performed in typical Phase III pivotal studies. This marked increase in time and effort makes it harder to recruit patients and keep them engaged throughout the trial, which in turn may have a substantial impact on research outcomes and costs[3].

The additional strain on patients from protocol complexity can affect maximizing site engagement and performance as well. Any disconnect between the sites and the protocol design can result in lower patient numbers and sub-optimal trial compliance, which may result in poor data quality and data variability.

In addition to complex designs, protocol amendments create difficulties for trial sites and add to sponsor costs. A study by the Tufts Center for the Study of Drug Development found that almost 50% of substantial protocol amendments are deemed avoidable[4]. Eliminating these amendments could reduce trial times by three months on average, while saving as much as $141,000 and

$535,000 spent on substantial protocol modifications for Phase II and III trials respectively, the Center suggested. It is therefore critical that sponsors proactively address the challenges of clinical-trial design, and consider how to optimize study protocols to boost patient and site engagement, enhance cost-effectiveness, and deliver compelling outcomes for regulators, patients and other stakeholders.

Why Protocol Design Matters

By Dr Nuala Murphy,
President Clinical Research Services, ICON plc

For a clinical trial to produce meaningful results, it must be designed to collect and analyze the right data. Amassing irrelevant data is burdensome to the site and patient and can overcomplicate research efforts, without bringing any real benefits in return.

A study conducted by The Center For Information & Study On Clinical Research Participation (CISCRP) in 2017 estimated that around 30% of data gathered in trials has no influence on any further stages of drug development[5]. The level of focus and investment required to collect unnecessary data would be better directed at more efficient and effective patient recruitment and engagement.

Another key challenge in protocol design is being more scrupulous about selecting endpoints that demonstrate treatment efficacy. Optimizing designs also helps sponsors predict disappointing outcomes at an earlier stage. They can then conserve resources and costs by making timely decisions about terminating trials that fall short of expectations.

A study published in the *Journal of Biopharmaceutical Statistics* in 2016 looked at unnecessary measurements in clinical trials. Typically, these studies have two or more primary endpoints, the authors observed[6]. Each additional endpoint increased medical costs and the number of measurements required. It was observed that it was also likely to result in a longer follow-up period. Furthermore, in any given sample size, the possibility of individual patients exhibiting each of these endpoints could vary widely, adding a further layer of complexity to determining efficacy.

Aside from data issues, there can be lack of alignment between investigators, sponsors and CROs over protocol design. This can have a ripple effect on patient recruitment and retention, since responsibility for patient engagement falls on the site investigator. Improving communication around protocol designs, and making them more patient-centric, ensures that research plans are more appropriate, user-friendly and productive. Exclusively scientist-designed protocols are not in the best interests of patients.

Optimizing Your Protocol

Protocol optimization calls for a combination of strategies, including data analysis, new technologies, and establishing channels for collaboration with patients. By addressing these challenges in clinical-trial design, sponsors will be better equipped to enhance patient recruitment and improve the engagement of patients and study sites alike.

Leveraging new analytical technologies enables mining of data from historical studies to explore potential road blocks in similar protocols. Rather than amending protocols to meet desired endpoints as the trial progresses, sponsors can establish a better-tailored design in advance through an initial review of protocol feasibility from operational, therapeutic and statistical standpoints.

Evidence from successful clinical trials suggests these are often characterized by common themes involving the study site and investigator engagement[7]. Drawing on information collated from other trials, sponsors can develop forecasts that anticipate research outcomes and minimize the need to amend the protocol once the trial is underway.

Contract research organizations (CROs) have access to vast amounts of data from studies conducted over extended periods, across multiple therapeutic areas, and in different indications. This rich repository of data is an effective means of informing and optimizing protocol development, by highlighting any potential hurdles and roadblocks to trial progress.

Patient Input

A research hypothesis with robust, measurable end-points is meaningless if the sponsor cannot recruit patients or volunteers and retain them over the duration of the trial[8]. A patient-centric recruitment strategy that focuses on motivation and engagement will support more positive outcomes.

Working closely with sites to gain patient feedback through surveys and focus groups to determine perceptions of clinical trial burden and attitudes of the patient experience enables sponsors to potentially amend the protocol in the earlier stages of trial design. These types of patient engagement can be used to develop patient-burden analyses which employ time-in-motion studies to measure the impact of each trial procedure on patients. The analysis can then be used to create a comprehensive matrix specifying the time commitment for each element of the protocol, along with recommendations to enhance patient-centricity. Additional surveys of the target patient demographic can explore attitudes to symptoms, study procedures and visit lengths, as well as their individual and collective influence on patients' willingness to participate in the study.

Involving investigators in review and development of the trial protocol provides another perspective, which could reduce site burden and lead to increased predictability in patient

recruitment.

Increased collaboration and communication between the sponsor, patient and investigator is more likely to deliver protocol designs that can be executed more effectively. It will ensure protocols are tailored to answer the right scientific questions, while also empowering investigators to recruit the most suitable and engaged patients.

These insights feed into recruitment and retention strategies that mitigate site and patient burden to drive on-time completion of clinical trials.

Conclusion

Protocol optimization can be instrumental in improving patient and site engagement to mobilize increasingly complex clinical trials. Insights from patients and investigators, coupled with data from historical studies enable sponsors to significantly boost both participant numbers and trial-site compliance.

A laser focus on protocol optimization improves the odds of successful, timely and predictable patient recruitment, while making sure the right data points are collected to deliver cost-effective clinical trials with more compelling study outcomes.

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