ASSESSING PATIENT AVAILABILITY:

Where Trials Go Wrong Today And How They Can Improve Tomorrow

The timely enrollment of patients into clinical trials is critical to productive development programs. Sites that efficiently identify, recruit, and retain clinical trial participants enable studies to finish faster, avoiding the costly and time-consuming overruns that blight trials. This makes knowledge of patient availability a valuable resource.

Calculations of the proportion of trial sites that never enroll a single subject range from the Tufts Center for the Study of Drug Development's 11% to Medidata Solutions' one-third.[1,2] Regardless of the actual figure, all evidence shows non-enrolling and under-enrolling sites cause delays and add to costs. An analysis of 151 Phase II and III global clinical trials run between 2008 and 2010 found more than 50% of studies failed to complete enrollment in the planned time.[3]

These issues are exacerbated by the high level of competition for sites and patients in some indications and the rise of drugs that target small subpopulations of patients. Both trends are illustrated by cancer trials.

As of September 2017, ClinicalTrials.gov listed 574 active clinical trials involving Merck's Keytruda and a further 471 studies featuring Bristol-Myers Squibb's rival checkpoint inhibitor Opdivo. This is a small subset of the total number of immuno-oncology clinical trials, many of which offer similar combinations of treatments to the same populations of patients. This presents a daunting burden on patient recruitment.

Sponsors typically turn to leading academic medical centers as primary clinical trial sites but this is unsustainable in some indications. The centers treat too few patients with some indications to meet enrollment demands, either because many sponsors are targeting the same indication or the drugs are aimed at very small subpopulations with certain genetic markers.

These factors create acute challenges for the successful development of certain types of drugs, but no sponsor is free from patient enrollment headaches. The aforementioned Tufts study found respiratory, cardiovascular, metabolic, and central nervous system clinical trials suffer even longer enrollment delays than oncology studies.

The inability of trials to retain all the patients they enroll aggravates the challenge of testing a drug in enough patients to generate meaningful data. The oft-cited median dropout rate is 30%. A recent assessment of trials in the United Kingdom put the average dropout rate at 11%.[4]

In some trials, the figure is notably higher and has a serious negative affect. The 40% dropout rate in a GlaxoSmithKline diabetes outcome progression trial made it impossible to rule out bias as the cause of differences in outcomes between the rosiglitazone and metformin cohorts.[5]

The burden placed on clinical trial participants significantly contributes to the high dropout rates. The burden on investigators and site staff has similar effects. Experienced and novice investigators alike drop out of the clinical trial system each year, due in part to burnout. This contributes to the lack of patient availability by reducing the number of qualified investigators.

The successful recruitment and retention of viable clinical trial patients and highly qualified and motivated investigators are long-standing challenges for the pharmaceutical industry. The ability to address the root cause of the issues and resolve them would have a major impact on global clinical research.

How Teams Assess Patient Availability Today

One takeaway from the ongoing enrollment challenge is that sponsors need better ways to identify trial sites with access to patients that meet their inclusion/exclusion criteria. Failure at this step in the process leads teams to activate rescue sites that never enroll patients. Yet, research shows many companies still rely on the tried-and-tested approaches that have served them poorly in the past.

Medidata's 2017 survey of clinical operations professionals found almost 70% of people work with country affiliates and local thought leaders to assess patient availability when designing clinical trials. The second most used approach is to base site assessments on the prior clinical trial experience of an investigator. These are subjective, time-worn approaches.

Similar patterns emerged when survey participants were asked how they determine whether patients will meet inclusion/exclusion criteria and how they assess site and patient burden. Again, almost 70% of respondents said they rely on country affiliates and thought leaders to validate inclusion/exclusion viability, with a high proportion noting that they still use subjective information to assess burden.

These responses are indicators that subjective insights derived from the protocol feasibility process continue to dictate study design decisions, despite repeated failures to meet the most conservative enrollment timelines.

Objective data may deliver better results. However, the survey shows few clinical operations professionals factor data into assessments of patient availability, the viability of inclusion/exclusion criteria, and the burden trials place on subjects and sites. One-third of respondents said they are not at all familiar with software that provides insights into patient availability. Only 3% of people currently use patient availability software.

Despite these low numbers, sponsors place significant value on data focused on patients with active disease and their proximity to potential trial sites. More than 80% of respondents said disease status and inclusion/exclusion criteria are critical or very important to patient availability assessments. About 50% of people placed the same level of importance on factors relating to the locations of patients.

The low uptake of technology reflects the lack of products that provide such data. Resources available today typically show where patients with a condition have existed historically. The dated nature of such data makes it less useful than near-real-time insights into the numbers of patients in the active disease state who meet eligibility criteria and their proximity to potential trial sites.

Without such up-to-date data, sponsors may continue to rely on subjective information.

What Teams Want From Patient Availability Software

The predominance of subjective information in patient availability assessments means there is considerable potential to improve efficiency through the use of analytical, data-driven approaches. Responses to the survey demonstrate there is pent-up demand for such approaches.

Two-thirds of the respondents familiar with patient availability software said their company would be likely to buy robust data sources and software. All of these respondents see at least moderate value in patient availability software. Half think such software has significant value. Only 13% of respondents said they see no need for data and software. Fewer than one-third of people think they would struggle to build a business case to justify buying these resources.

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The question is, what improvements need to be made to patient availability software and the supporting data assets to persuade more than 3% of clinical development professionals to deploy these tools? One way to answer this is to look at the areas in which high-quality data is lacking today.

About two-thirds of respondents singled out a lack of information about competing trials being run by investigators as a problem today. A similar proportion of people said there is a dearth of insight into whether patients will meet inclusion/exclusion criteria. More than half pointed to the need for data to be more accurate and timely as a major shortcoming of today's resources.

The survey also shows clinical operations professionals need better resources to assess the burden clinical trials place on patients and sites. Almost 90% of people indicated being able to assess the burden imposed on patients during the conduct of a clinical trial will significantly aid in retention over the full duration of the study.

There is a lack of objective resources to support these assessments. Most protocol authors and feasibility specialists rely on internal intelligence, potential investigators, and key opinion leaders for information. A minority use internally or externally developed analytics to support their development strategies. Almost 10% make no attempt to measure site or patient burden as part of their feasibility process.

Technology that supports insights into the competitive landscape of concurrently enrolling trials may provide a window into the potential for patient eligibility and is likely to find favor with the life sciences industry. However, the survey identified red lines that would deter the adoption of otherwise useful patient availability software and supportive data assets. Integration with internal systems and cost were noted as key concerns for at least half of those surveyed.

New Opportunities To Reduce Enrollment Challenges

These are significant but manageable concerns. Importantly, very few respondents voiced insurmountable objections to the use of data and software. The concerns are technical in nature, but not fundamental doubts about the need for or value of objective insights. This is an encouraging sign for the future of patient recruitment and retention, particularly when viewed in light of the very low rate of technological penetration today.

Sponsors are still trying to answer what is essentially an objective question — where are the patients? — with subjective information. If technology companies provide sponsors with robust data and high-quality analytical tools, there is reason to hope the recruitment and retention problems that have dogged the industry for decades will diminish.

References

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