PRA Health Sciences

WHITE PAPER

Multi-Stakeholder Collaborations Can Minimize Barriers & Drive Rare Disease Clinical Programs to Better Patient Outcomes

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Executive Summary

Conducting clinical trials in rare diseases and advancing research pipelines requires a collaborative, multi-stakeholder approach. The process requires cooperation from industry, academic researchers, advocacy groups, and patients as well as their caregivers and families. Each stakeholder brings a different perspective to the conversation. Listening to their voices and engaging stakeholders early in study design planning, positioning of the trial, and engaging with patients may minimize barriers and drive clinical programs to better patient outcomes. Building trusting collaborative relationships that are mutually beneficial contributes to increasing study awareness and strengthens the common goal of advancing therapies and getting new therapies to the market faster.

In this white paper, we look at the barriers drug developers face when positioning a new trial in the rare disease space and how to minimize these barriers by applying a multi-stakeholder collaborative approach to drug development.

Introduction

Historically, drug development in rare diseases, also known as orphan diseases, have not received the same level of attention or the research and development funding as other indications (ie, oncology). Rare disease trials often involve smaller patient populations, and the overall public health benefit is perceived as more limited than for common indications. Drug developers have focused on developing therapeutics for common diseases that affect larger patient populations and yield a better return on investment. However, this focus is shifting as we develop more targeted therapies and as we better understand the etiology of many rare diseases. Although orphan drugs target smaller patient populations, they have become commercially attractive for several reasons: the higher cost of therapy, government incentives, typically smaller and shorter trials, extended exclusivity, and favorable regulatory scrutiny.

The approach to rare disease drug development is evolving and recognizes the value of input from a variety of stakeholders. Patients and advocacy groups are now taking a more active role in the process, whereas in the past they were "just" participants.[1] These stakeholders understand the barriers patients face and can provide insights into minimizing them. A multi-stakeholder collaborative approach is critical to advancing therapies for patients with rare diseases.

What are the Barriers for Positioning New Clinical Trials in the Rare Diseases Space?

Accessing sufficient suitable patients and retaining them throughout the course of a study are significant barriers for drug developers. Certain indications have especially challenging diagnostic hurdles; diagnostics can play a significant role in identifying suitable patients. Conducting natural history studies and creating patient registries can help drug developers determine where these patients are and what the early stages of the disease process look like. These studies can also help to define the course of a disease and to assist in the selection and validation of appropriate endpoints. This information is valuable when designing a study, selecting endpoints and outcome measures, and identifying suitable sites and geographies.

Furthermore, many rare indications are new entities that are being discovered as diagnostic technology and insights within the industry improve. Endpoint design and selection can be challenging because little is known about these indications and there may be no established benchmark; endpoint selection and the identification of surrogate endpoints or biomarkers is critical. Endpoint selection should be partly driven by asking what will make a difference to patients and their families. These stakeholders offer unique perspectives and can help create a successful clinical program.

How do Multi-Stakeholder Collaborations Drive Rare Disease Clinical Programs?

Aligning key stakeholders increases study awareness, mitigates potential barriers, incorporates the patient perspective, and drives strong scientific outcomes.

Investigators

Investigators are drug developers' most important partners; they are the most important ingredient, as they enroll patients and engage key opinion leaders (KOLs) and other investigators. When identifying investigators, look for those who see the most patients and who have published in the area. Information is available through pharmacy claims and other public data sources. Be selective and demanding and assess previous performance when choosing investigators. Sites that do not enroll patients or that do not increase visibility among the treatment community will impede study progress. Approximately 25% of sites never enroll a patient once they are activated. To eliminate this huge inefficiency, select sites that will enroll based on performance data.

Some factors to consider when identifying potential investigators include availability, resources, existing workload, completing trials, and accrual history. These key variables can be used to rank investigators and select the best sites. However, in situations where the anecdotal experience of KOLs is unreliable, apply the "Lasagna Rule" of patient recruitment: Typically, take one-third or one-half of what a KOL estimates to derive a more realistic enrollment number.

It is beneficial to leverage the study sponsor's relationships with investigators, as they already understand accrual history, thought leadership, and general leadership for a study down to the level of details that can facilitate enrollment. Contracts may already be in place with a site, and the ethics committee submission process is understood; these factors can speed study start-up and accelerate the start of enrollment.

Patient Advocacy Groups

Patient advocacy groups are critical stakeholders in any clinical development program. Some advocacy groups are vocal and mature, and may possess significant resources and knowledge. They play a significant role in helping drug developers understand the disease and patient pathways and provide insights into the needs of patients and their families. Advocacy groups provide several benefits:

- Raise study awareness
- Encourage patient enrollment and retention
- Guide study design
- Motivate researchers
- Connect industry with patients

Advocacy groups are open to relationships with industry; they want transparent and honest relationships with drug developers and they want them to remain involved in the disease community over the long term as a resource, not just to enroll their clinical trials. Engage with them by asking them to describe the ideal partner. By being supportive, drug developers create trust and reinforce study branding. Study timelines may benefit from endorsements from patient advocacy groups. The opposite is also true; there are instances in which industry has not partnered well with disease-specific groups, and trials and development programs have almost been halted.

Locating advocacy groups is easy because they are so visible. Try to align selected sites and investigators with the advocacy group's location to facilitate partnerships. This creates a multi-faceted partnership between investigators, advocacy groups, and patients.

Patients

Patients are a key partner in the clinical trial process. Many patients are open to participating in clinical trials and have a strong sense of altruism. It is nevertheless important to understand what patients, caregivers, and families are seeking in a clinical trial and what would make a difference in their life. One way to capture their voices is by conducting a feasibility study.

Feasibility feedback helps drug developers identify patients and understand their needs, concerns, and interests and what is realistic in terms of potential participation in a clinical trial. The information is an exceptional guide on how to engage

patients so they become an active part of the trial or an advocate to others who are considering it. A good way to identify the right patients and groups is to determine whether patient registries exist in the space. Registries can be a great resource for understanding where patients are and for hearing about their experiences.

Clinical Research Organization

As drug developers are moving a clinical development program forward and have lined up investigators, patients, and advocacy groups, clinical research organizations (CROs) bring these various parties together. Selecting the right CRO partner is as important as engaging capable investigators, the strongest advocacy groups, and the right pools of patients.

Knowing which CRO is the right fit for a trial depends on several factors, for example: organizational size, therapeutic expertise, indication experience, reputation, past performance, price, etc. Balancing the right mix of therapeutic expertise and experience with breadth of coverage are top considerations for most trials in rare disease indications.

Having a partner with geographic reach and staff in the countries of interest is important to both the operational perspective and regulatory timing and processes. Knowledgeable partners prevent stakeholders from being blindsided by an unforeseen obstacle as the first patient is about to enroll. It is critical to choose a partner who understands the level of detail involved in each of the country-specific steps and timelines.

The best clinical development partners for rare-disease trials understand that these trials are quite different for many reasons. Working with a group that understands these differences, knows how to overcome the hurdles, and has direct experience is imperative to executing a successful study. When considering CRO partners, ask about experience and lessons learned in previous studies. CROs should be able to apply those lessons learned to a program and conduct the study more efficiently as a result.

Ultimately drug developers seek a CRO partner to accelerate their trial. The CRO should be able to forecast timelines for site recruitment, country activation, and patient enrollment. The ability to forecast these parameters, anticipate hurdles and risks, and develop contingency plans are the tools of the successful CRO partner.

Summary & Recommendations

Drug developers face many barriers when conducting trials involving rare disease patients. Taking a multi-stakeholder collaborative approach to the planning and execution of these trials is critical. Developing long-term, transparent, honest, and mutually beneficial collaborative relationships among all stakeholders will help drug developers achieve their goal of bringing treatments to rare disease patients faster.

Citations

1. The Must-Have Collaborations for Successful Drug Development; https://globalgenes.org/wp-content/uploads/2015/03/Drug-Development-White-Paper-2015-FINAL.pdf

Contact Information

Are you aware that the approach to conducting clinical trials in rare disease patients is different and requires the involvement of all stakeholders—including the patient? If not, it may be time for you to look for a trusted partner with experience and expertise managing studies in rare diseases.

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