Integrative Approach to the Conduct of Rare Disease Clinical Trials

The planning and execution of rare disease clinical trials involves unique considerations. Examples include the role of patient advocacy groups, the value of outcomes registries and complete natural histories, the challenge of recruiting and retaining study participants, the special qualifications of investigators and clinical sites, unsettled clinical endpoints, and the variable availability of outcome assessment tools. Add to this a wide cast of participants including patient advocacy groups, specialised academic investigators, genetic counsellors and other medical experts, home nursing support companies, recruitment specialists, and communications experts – and the challenge of integrating and coordinating all these elements becomes apparent.

Patient Engagement in Rare Disease Clinical Trials

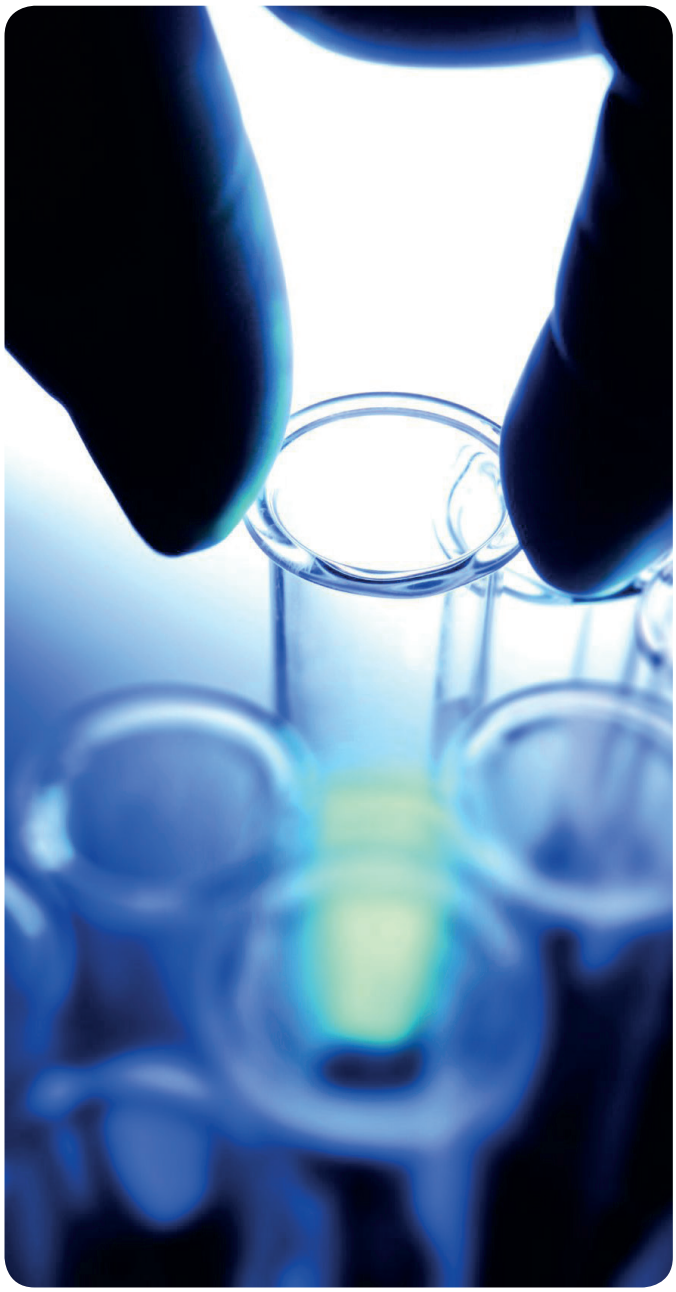
The most important participant in a rare disease clinical trial is the patient. The patient experience is central to the successful conduct of the clinical trial. Patient engagement acknowledges that patients and their families want to be recognised as partners throughout the lifecycle of research and therapy development. Recognising the patient's voice might include facilitating their access to a clinical trial site or anticipating their logistical needs or disease specific burdens and addressing them within the protocol.

Patient advocacy groups, support groups, and disease associations can give voice to valuable information about patient needs, desires, points of view, and treatment networks. Engaging with these groups ensures that patients' voices are heard throughout the development of the clinical protocol. Rare disease patients may have preferences with regard to burden and frequency of clinical assessments; how they communicate with study clinicians; and how they can influence the endpoints, outcomes measures, and study design so that they are most meaningful.

Collaborative Relationships Drive the Patient-centred Approach

Understanding the challenges of coordinating all the parties that enable a high-quality patient experience and the generation of robust data are central to an integrative approach. Focusing on the rare disease patient is underpinned by strong medical, operational, and regulatory science, and driven by productive relationships between investigative sites, treating physicians, patient advocacy groups, academic thought leaders, and corporate sponsors.

A critical point of contact for many of the groups needed to successfully design and execute a rare disease



trial is the clinical research physician specialist who typically resides in the sponsor or the clinical research organisation (CRO). A close relationship between the study physician and the site principal investigator leverages shared training and a passion for patients. The result is effective collaboration during protocol design and later, during the clinical trial, as the inevitable questions, issues, and obstacles arise. This close relationship is particularly important during any long periods between subject enrolment. It can also cut down on protocol violations or needless amendments, and it can ensure that no opportunities to enroll have been lost.

If a CRO is operationalising the study, a tight relationship between the clinical research study physician and sponsor study physician ensures connectivity between the sponsor and investigational sites; moreover, it is vital for timely review of emerging study data so that protocol adjustments can be made with agility. And a strong collaborative relationship among industry physicians and scientists, treating physicians, and academic thought leaders is critical not only for benefiting from their direct experience but also for sharing insights from cross-sponsor clinical research in their area.

Collaboration with patient advocacy groups and key academic investigators is the most effective way to identify protocol-eligible patients with a specific rare disease. These patients may be geographically sparse, in the case of ultra-rare diseases, or clustered in a few geographies due to genetic inheritance patterns.

Conclusion

Executing clinical trials in rare diseases have more in common with each other operationally than a rare disease like cystic fibrosis might have with another disease in its therapeutic area, such as asthma. Approaching rare disease clinical research by acknowledging this commonality helps make the planning and conduct of clinical trials more efficient. Cystic fibrosis and muscular dystrophy both require enrolment of paediatric populations, the need to interact with a parent caregiver, investigators who are usually in academic centres, etc. On the other hand, the biology underlying many rare diseases is poorly understood, and this can complicate the kinds of assessments and outcomes measures to be incorporated in a protocol.

Integrating and coordinating physicians and scientists with expertise in rare diseases, operational experts, regulatory affairs specialists, epidemiologists, and reimbursement specialists accelerates the speed and efficiency of rare disease clinical research. This sort of approach ensures a holistic view of clinical trial planning and execution, and harnesses the passion and science of all stakeholders toward the goal of improving the lives of patients with rare diseases.

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