A multi-pronged and customized approach to rare disease clinical trial patient identification and recruitment

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A clinical trial offers hope for individuals and families impacted by rare diseases, often in situations where there are no existing treatments. Early diagnosis and access to treatment provides the best opportunity for these individuals to experience the benefits, such as slowing disease progression and improving their quality of life. As an industry dedicated to accelerating the development of new treatments to address unmet medical needs, it is essential for *every* individual affected by a rare disease to be given the opportunity to participate in clinical trials that could offer promise for them and their families.

Industry perspective

The biopharmaceutical industry has been rising to the challenge of developing treatments for rare diseases since the passage of the Orphan Drug Act in 1983 and now one-third of all drugs in active research and development worldwide target rare diseases.[1] However, clinical researchers face unprecedented challenges with patient identification and recruitment for these clinical trials across all phases of clinical development.[1] "Although collectively there are around 7,000 different rare diseases that affect more than 300 million people worldwide, identifying individuals affected by each specific indication and ensuring access to clinical trials is not straightforward. A customized approach that is founded upon intimate knowledge of the therapeutic landscape and patient journey is instrumental for every rare disease clinical trial," says Sarah Glass, Ph.D., Global Head of Rare Diseases at Parexel.

Traditional methods for recruiting patients into clinical trials—conducting feasibility surveys, launching multiple sites across multiple regions, and

waiting for patients to enroll—are only the beginning for rare disease clinical studies. Since the diagnostic and treatment journey of each rare disease patient is unique, a comprehensive and proactive approach is needed for identifying and recruiting them for these potentially life-altering clinical trials. This comprehensive approach can include multiple components, such as:

- Precision medicine
- Leveraging data-driven insights
- Proactive engagement with medical specialists
- Fostering relationships with patient and advocacy networks
- Designing patient- and caregiver-centric trials
- Seamless integration of technology, vendors and processes

Precision Medicine

Since 8 in 10 rare diseases are caused by a faulty gene,[2] state-of-the-art genomic tools are helping to accelerate rare disease diagnoses so that patients may have the opportunity to participate in clinical trials much sooner than they have in the past, or at birth in the case of infant-onset rare or genetic diseases.

Translational medicine experts take pharmacokinetic (PK), pharmacodynamic (PD), biomarker, and genomic data to help inform clinical development strategies and guide drug development decisions. Using deep knowledge of the mechanism of action regarding the drug and disease, geneticists, clinical pharmacologists, and biochemists can help answer critical questions along the entire drug development process to predict and optimize outcomes for patients, such as:

- How does genomic variation impact feasibility and site selection?
- Which biomarkers are relevant for selecting or stratifying patients?
- What are the inclusion and exclusion criteria for the intended patient population?
- What is the proper dosing strategy for this special population?

Data-driven insights

Data-driven insights are critical in helping companies determine the epidemiology of specific indications of rare diseases. Big data and analytics help companies visualize disease prevalence across the globe, focus their search within the right geographic regions, and identify treating physicians. Those results alone, however, are not enough to ensure successfully identifying, recruiting and enrolling a statistically relevant number of patients for that trial. Data shows that 81% of patients screened for rare disease clinical trials are not eligible to enroll and 56% fail to be randomized.[3] In order to identify a sufficient number of patients to mitigate those recruitment failure rates and still meet recruitment targets, a more customized and targeted outreach is required.

Proactive outreach

Data can pinpoint where to start researching and reaching out to treating physicians, key opinion leaders (KOLs), and specialist networks who educate, treat, and support that rare disease patient. “Since each patient’s journey is unique, these experts can

share the patient's experience that preceded their diagnosis and what their needs are, help optimize the protocols for these specific trials, and offer insight into the best strategies for recruiting them," says Shipra Patel, M.D., Global Head of Pediatrics at Parexel. For instance, a treating physician or KOL could inform patient identification of infants affected by a rare disease and whether this identification should start during pregnancy or after birth. Peer-to-peer discussions about the rare disease patient's journey and ongoing engagement with these medical professionals can establish the credibility of a biopharmaceutical company and build champions for their clinical trials.

Fostering relationships with the patient's network

Partnerships with rare disease advocacy groups, organizations that maintain patient registries, and patient and caregiver support networks demonstrate the commitment of the biopharmaceutical industry to the development of new treatments and cures. Cultivating ongoing relationships with a broader network helps establish trust with patients and caregivers. Direct patient and caregiver feedback, which helps the biopharmaceutical industry more fully understand the burdens these families face, can be used to select appropriate endpoints and design better protocols.

These long-term relationships with advocacy groups and support networks impact not only study design, but also help the biopharmaceutical industry improve patient care and experience from the earliest stages of drug development through treatment and beyond.

Patient- and caregiver-centric study design

As rare diseases often affect the entire family, it is important to grasp the challenges a family faces in living with that disease and participating in a clinical trial. "Rare disease patients and their parents or caregivers experience unique burdens that need to be recognized and addressed by the biopharmaceutical industry," comments Altair Silva, Director of Patient Recruitment at Parexel. "Reducing those burdens is essential in recruiting and retaining those patients." For example, as 50% of rare disease patients are children, site visits for them and their

parents or caregivers may have a considerable impact on school and work schedules. Considering that rare disease patients in a clinical trial have been shown to undergo 68 different procedures when compared to 30.2 for non-rare disease oncology indications,[3] frequent clinic, hospital or specialist visits may place significant travel and financial burdens on the family.

A patient-centric design, which involves placing patients and families at the heart of every decision, is achieved by gathering and using patient and family insights to modify study design and conduct across every stage of a clinical trial. Reducing complexity, logistical challenges and costs associated with clinical trials improves recruitment and retention of rare disease patients. A patient-centric protocol should consider trial designs (e.g., virtual trials, adaptive designs, crossover trials) that can simplify the study without compromising the quality of clinical data collected. Being patient-centric also means selecting endpoints based on efficacy and other relevant clinical outcomes measures such as time to remission, improved quality of life or fewer side effects. It means reducing travel burdens by considering telemedicine, in-home sample collection, and in-home assessments.

Parexel's Patient Innovation Center features a dedicated team that strives to reduce the burden of clinical trials for the patients and simplify and accelerate their journey to new treatments. Some solutions include:

- Reducing the number of study visits
- Supplying and supporting study-related technology
- Providing home visiting nurses and/or patient travel support
- Developing engaging patient information in their preferred format to keep them motivated

A more patient-centric study design can be achieved by using a formalized protocol optimization platform and process to incorporate patient and caregiver needs, views and experiences. This engagement with patient networks, families and caregivers must occur early in the trial design phase so that the insights may be fully considered and applied to protocol development. Research has shown that recruiting patients for rare disease trials using a patient-centric approach can reduce recruitment time by 40% compared to non-patient-centric trials.[4]

Seamless integration of technology, vendors and processes

A common approach in the biopharmaceutical industry is to use a number of different technologies, processes and vendors to accomplish specific functions in a clinical trial—e.g., electronic clinical outcome assessment (eCOA) technology for sites and patients, technology support, patient travel support, and patient reimbursement programs, to name a few. From a patient and caregiver perspective, the various processes and interactions can appear disjointed and add to the patient and caregiver burden. Centralizing patient-related interactions and services, from informed consent, to travel arrangements, telemedicine, technology support and more, helps improve the clinical trial experience for patients and their caregivers. This integration of technology, vendors and processes is helping drive both patient-centricity and site-centricity across the industry.

Conclusion

Research and development investment in rare disease treatments continues to grow and challenges remain in the global identification and recruitment of eligible patients for specific indications with a low disease prevalence. Leveraging precision medicine, data-driven solutions and collaboration across the rare disease community are instrumental when developing a customized strategy for patient identification and recruitment. Through this approach, the biopharmaceutical industry will be poised to ensure that every individual affected by a rare disease is given the opportunity to participate in clinical trials and that no patient will be left behind.

1. Tufts Center for the Study of Drug Development, Tufts CSDD Impact Report, July/August 2019.
2. Global Genes, Rare-Facts, globalgenes.org/rare-facts/.
3. Tufts Center for the Study of Drug Development, Tufts CSDD Impact Report, Jan/Feb 2020.
4. The Innovation Imperative: The Future of Drug Development, Part I: Research Methods and Findings, The Economist Intelligence Unit Ltd., ©2018. All rights reserved.

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