RARE DISEASE CLINICAL RESEARCH: STRATEGIES FOR ENSURING ENDPOINT INTEGRITY

Rare disease clinical trials can be particularly challenging when it comes to endpoints. Not only are there typically a limited number of patients that can be included in the trial, but often the endpoints themselves are novel or complex. Collaboration between subject matter experts at Medpace and ATOM International has resulted in better training and improved data visualization, pattern detection, issue prevention, and problem solving in rare disease clinical trials.

Medpace has collaborated with ATOM International for years in order to optimize clinical trials for neuromuscular and metabolic rare diseases, as well as clearly define and execute trial endpoints including respiratory and physical function measurements. ATOM International works predominantly with patients experiencing neuromuscular disorders, including Duchenne muscular dystrophy, Becker muscular dystrophy, spinal muscular atrophy, limb girdle muscular dystrophy, fascioscapulohumeral muscular dystrophy and myotonic dystrophy. They also support trials for glycogen storage disorders such as Pompe disease and Fabry disease, as well as the mitochondrial disease thymidine kinase 2 deficiency, an emerging treatment group. Studies of achondroplasia and skeletal dysplasia have also been included in these clinical trials.

CLINICAL TRIAL ENDPOINT DEVELOPMENT AND QUALITY CONTROL IN DATA COLLECTION

The first clinical trial in neuromuscular disease began in 2007. “Now the field has expanded exponentially to the point where we have over 40 trials in this area,” says Meredith James, the master physiotherapist at ATOM International. “At that time, the disease-specific endpoints or outcome measures were not available,” explains James, “and we were just running with what we had.” Over the past 13 years, James and her team have developed a package of standardized training and manuals on how to collect endpoint data. They now have clearly defined disease-specific endpoints, as well as a wealth of training materials.

ATOM are involved in trials from the outset and are able to provide advice on endpoint selection. ATOM provides consultation on protocol development, target population inclusion and exclusion criteria, endpoint information, guidance on endpoint selection and development of a clinical manual of operations in order to standardize the collection of data throughout the different clinical trial sites. Since most of their studies are global, training all clinical evaluators (CEs) who will be collecting data on primary and secondary endpoints is extremely important. The ATOM team relies on Medpace’s clinical operations and data management team to jointly develop their source documentation to ensure alignment with protocol and electronic case report forms.

Quality control is essential to rare disease clinical trials. A good outcome measure is reliable, repeatable, and standardized. It is also sensitive enough to measure change over the period that the trial is set. ATOM has developed standardized training procedures and manuals of operation with Medpace as their operational partner to ensure that the variation in the data is minimized, and that the changes detected are true changes.

Medpace provides operational support for ATOM to conduct both in-person and virtual novel endpoint trainings around the world and supports execution of these endpoints with standard calibrated equipment. Medpace has developed a standardized electronic case report form (eCRF) library, data reports and data visualizations for many of these disease-specific endpoints, which is crucial to the success of rare disease clinical trials, as it facilitates the data collection and presentation at review meetings.

PLANNING A RARE DISEASE STUDY

Medpace's data management team and the ATOM International group review study data periodically during each trial to detect any signals that could indicate issues with test administration by the clinical evaluators at the trial sites. The teams collaborate during quarterly data review meetings, reviewing data listings as well as subject profiles including demographics, adverse events, concomitant medications and any other factors that may affect the clinical evaluator tests. Data visualizations help to identify errors or trends as quickly as possible.

"One of the most important paths to success when executing complex endpoints is to build systems with your plan in mind," says Michelle Petersen, Senior Director of Clinical Trial Management at Medpace. Endpoint integrity is enhanced when patients complete procedures in a specific order so that impact from fatigue and other factors are properly controlled. Early protocol collaboration ensures that the best endpoints are selected and that they are reasonable for site staff to conduct. For example, strategically conducting important endpoint testing earlier in the day ensures the patient's abilities are accurately captured. Medpace's focus on optimized communication between ATOM trainers and site staff can accelerate study start-up, ensuring that training is complete ahead of initiation of enrollment. Finalizing training manuals and supply requirements early in the study start-up process allows adequate time for site preparation, budget evaluation, and language translations.

Medpace has created a cross-functional rare disease certificate program so that all team members contributing to rare disease studies benefit from their institutional knowledge and innovation. CRAs are highly trained and encouraged to build positive relationships with trial sites in order to promote open, honest and timely communication. CRAs act as the first-line contact for site staff. Detailed training empowers the CRA team to answer site questions quickly and efficiently, reducing the likelihood of delays or errors in patient assessments.

EFFECTIVE CE TRAINING FOR GLOBAL CLINICAL TRIALS

A global reach is often necessary to obtain the required sample size for a clinical trial involving a rare disease. Medpace and ATOM work to ensure the site Clinical Evaluators who perform critical procedures to support study endpoints are properly prepared. The team ensures translators are available for investigator meetings, virtual and on-site training as needed. ATOM's Master Physiotherapists are strategically based in 7 countries to ensure support is available to sites around the clock. Medpace CRAs are regionally based and are available to support ATOM trainings in local languages. ATOM and Medpace share in the goal of ensuring site staff are fully trained and capable to conduct a successful clinical trial.

Medpace continues to work towards this continuous improvement cycle to deliver the best trials possible for their patients and research partners.

FULL-SERVICE CLINICAL DEVELOPMENT

Medpace is a global full-service clinical research organization providing Phase I-IV core development services for drug, biologic, and device programs. With medical and regulatory expertise in multiple therapeutic specialties. Medpace has assembled therapeutically focused teams to execute at every level of the company's operations, providing complete and seamless drug and device development services.