Elevate your neuromuscular clinical studies with Fortrea's specialized expertise and comprehensive support

Contributors

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Operationalizing complex, rare neuromuscular clinical trials

Successfully navigating rare neuromuscular clinical studies is no small feat. Neuromuscular disorders, affecting both children and adults, typically require complex study designs that require thoughtful planning and execution, including appropriate site selection to facilitate patient recruitment and careful oversight to ensure precise endpoint assessments. The large unmet need for effective treatments in this area requires a well-strategized approach to get it right the first time.[1]

Rare neuromuscular trials present challenges that impact sponsors, patients and their families, and study sites, necessitating a comprehensive, collaborative and well-coordinated approach to trial execution. Thus, operationalizing these studies demands a deep understanding of the intricacies involved. Given our experience in this area, which includes a portfolio spanning pediatric, adolescent and adult populations, and with modalities including small molecules, biologics and therapies, we aim to provide valuable insights into the successful execution of these complex studies.

Site selection: nurturing academic talent

Problem: Selecting the right-fit of a study site is paramount for the success of rare neuromuscular studies, as the assessments for these studies require specialized expertise and facilities. The number of sites, investigators and physiotherapists with this adept level of expertise are few, and those who have it are often participating in numerous, demanding trials involving diverse neuromuscular diseases.

Solution: A) Investing in academic researcher career development, **B)** empowering investigators with foundational good clinical practice (GCP) training and educational discussions with the medical monitor and **C)** pairing him or her with a seasoned clinical research associate (CRA) can set the stage for success.[2] For example, we selected an investigator with 20 years of academic investigator-led research to participate in a registrational neuromuscular study, supported by a senior-level CRA to ensure compliance and quality. This has become one of our most high-performing sites.

TIP: Ensure you have tailored CRO support, leveraging partnerships with vetted academic researchers who may be new to industry research.

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Academic-based vendors: cultivating collaborative partnerships

Problem: Academic vendors who provide centralized muscle MRI, functional testing or specialty laboratory services play a pivotal role in neuromuscular clinical research, contributing invaluable insights and skills. However, their deliverable timelines may be dictated by their clinical schedules and responsibilities outside of vendor tasks.

Solution: CROs should nurture close relationships with these partners, flattening CRO oversight team hierarchies to provide high-touch service and tailored solutions. The CRO should also provide complimentary project management and logistical support as needed. For example, by creating a successful collaborative relationship with an academic vendor, we enabled a more comprehensive review of critical endpoint data, making the endpoint protection process more impactful and meaningful.

TIP: CROs should maximize the potential of academic vendor collaborations by adapting standard vendor management structures to "fit" the vendor and by offering additional logistical support as required.

Recruitment and foreign patient planning

Problem: Patient recruitment for rare neuromuscular studies often transcends geographical boundaries. Recruiting foreign trial participants adds complexity that must be addressed through proactive planning and an approach that is both patient- and family-centric. This is particularly important for children because their caregivers must facilitate site visits.[3]

Solution: Feasibility assessments and partnerships with patientadvocacy groups (PAGs) can facilitate opportunities for cross-border participation. Utilizing strong patient advocacy connections will allow for the engagement of patients directly and facilitate logistical discussions. CROs should have deep nation-level knowledge of necessary approvals (e.g., visas), vendors and logistical expertise to facilitate inclusive and impactful research across country borders. Cross-border study participation is most commonly seen between European (EU) countries and Canada/U.S., but we have also supported long-distance travel from Africa and South America to the EU and U.S., respectively. Working closely with country-specific PAGs, the sponsor and our travel vendor, we identify the most patient-friendly plan, while also ensuring financial coverage is appropriately addressed.

TIP: Managing international patients—including children and patients' families—should involve creating personalized plans that address logistical challenges and ensure low-burden participation across borders within an anticipated travel budget.

Equipment suitability: ensuring endpoint precision

Problem: Fit-for-purpose equipment at investigational sites is paramount in ensuring the reliability of study endpoints. Inappropriate equipment can lead to unusable data and impact the study's validity.

Solution: Prioritize the identification of appropriate equipment upfront to support high-quality data, as inappropriate equipment and/or testing conditions are important sources of variability. For instance, when assessing requirements for Performance of Upper Limb (PUL) 2.0, we discovered that sites were conducting the PUL without an appropriate table to accommodate wheelchairs, so we sourced and provided appropriate tables.[4] Similarly, we provide sites with the correct plinth tables for the North Star Assessment for Dysferlinopathy (NSAD) assessment, avoiding the use of inappropriate equipment like soft hospital beds, which can negatively influence NSAD scores.[5]

TIP: A CRO should ensure the reliability of your study endpoints by proactively reviewing site functional equipment and testing conditions, during prestudy visits and then a site-specific walk through of procedure conduct at site initiation visits.

Spirometry

Problem: Spirometry assessments present unique challenges due to strict criteria that may not align with patients' capabilities, often leading to false exclusions.

Solution: Take a patient-centric approach, reporting all spirometry values and considering adjusted standards during analysis to prevent false exclusions. For example, in neuromuscular diseases, patients often require more back extrapolation due to their condition, which needs to be accounted for in the criteria for acceptable spirometry quality.

TIP: Design spirometry measures and select vendors appropriate to patients with neuromuscular diseases; this ensures accurate measures and prevents false exclusions based on overly strict spirometry criteria.

Muscle MRI

Problem: Most imaging vendors for clinical trials do not possess robust experience in neuromuscular imaging, which may lead to suboptimal images and difficulties interpreting the data. The most experienced muscle MRI vendors are often academic based or originated from an academic setting, and these vendors may require more logistical support, as previously discussed.

Solution: Prioritize the selection of experienced vendors to ensure accurate interpretation of muscle MRI data. Selecting a vendor with expertise in site qualification, image acquisition and central review of images is crucial for reliable data collection and analysis.[6] Experience with managing the study's patients is equally important, as on-time patient scheduling and patient-friendly approaches to minimize the burden associated with MRI scans is crucial.

TIP: When using MRI as an endpoint, choose experienced vendors with a deep understanding of the intricacies of muscle involvement in neuromuscular disorders to ensure an on-time, positive patient experience with reliable data collection and analysis.

Biopsies: needle vs. open biopsy

Problem: Biopsy procedures can be intimidating and uncomfortable for patients—particularly adolescents—and that can impact their assent for participation. Interestingly, we have seen better acceptance of open biopsies than needle biopsies, which are less invasive. This is due to the intense fear some patients have of needles.

Solution: Put patient comfort and safety first, offering alternatives such as open biopsies under general anesthesia to alleviate fear and discomfort. Allowing investigators to choose the option that aligns best with patient preferences and standard of care enhances patient participation. It is also helpful to provide age-appropriate comfort aids and distraction aids for children and adolescents to ease their fears prior to the procedure.

TIP: When considering biopsy procedures, explore options to address patient concerns about needles and pain; provide support materials well before the biopsy to allow time for the patient to become more comfortable with a procedure they may find scary.

Monitoring functional endpoints and clinical evaluator changes

Problem: Drastic swings in functional outcome measures can occur due to frequent changes in clinical outcomes assessors or varying equipment used during assessments.

Solution: Ensure consistency in evaluator training and equipment use throughout the study. For example, instructing sites on proper equipment use and maintaining inter-rater reliability can stabilize outcome measures.

TIP: CROs can ensure consistency in functional endpoint assessments by ensuring appropriately trained back-up staff, and by maintaining stable clinical evaluator teams and standardized equipment throughout the study.

Choosing the right neuromuscular clinical study partner

Operationalizing complex, rare neuromuscular clinical studies demands a multifaceted approach focused on collaboration, patient centricity and proactive problem-solving. We have a long track record of excellence in this area, addressing challenges such as site selection, vendor collaboration, patient recruitment, equipment suitability and endpoint protection. By investing in academic researcher development, fostering vendor relationships and leveraging patient advocacy, we ensure every aspect of your trial is personalized for successful execution.

Contact us today to learn how Fortrea can proactively execute your rare neuromuscular clinical study.

See how we can help.

Together, exceptional is possible

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