Case Study:

INNOVATIVE OPERATIONAL STRATEGIES TAILORED FOR NEURODEGENERATIVE TRIALS

BACKGROUND

80 PARTICIPANTS

20 SITES

This case study highlights how targeted operational strategies enable efficient recruitment and optimized study design in a complex trial of a genetically defined neurodegenerative population implemented across three geographically dispersed regions.

CHALLENGES	SOLUTIONS
• Recruitment of a genetically defined neurodegenerative population requiring targeted identification and screening to locate participants with specific, less common genotypes	• Offered comprehensive feasibility exercise • Coordinated site outreach/KOL engagement by Operations and Medical • Utilized global multicenter recruitment • Implemented parallel genetic testing program • Established experience for cross boarding participants

• Placebo controlled design in a progressive disease study presents ethical, methodological, and practical challenges, for example:
  • Holding potentially beneficial treatment in a rapidly progressive and fatal neurodegenerative disease
  • Placebo allocation may be a recruitment and retention hurdle
  • Separating the effect of the investigational drug from background treatments
	• Included patient and public involvement in study design and conduct
	• Required to be on standard of care as part of eligibility criteria
	• Created the option to access investigational product in open-label extension with flexible eligibility
	• Study design maximized active product allocation and potential to supplement placebo arm with external controls
	• Conducted stratification and baseline treatment adjustment in the analysis models

• Significant number of vendors (e.g., COA, labs, imaging, other assessments, translation) creating operational complexity, requiring additional coordination, and collection of data from different sources with possible impact on data integrity and quality resulting in an impact on study timelines	• Defined data transfer specifications early in the study • Delivered site and rater training, including qualifications and stability supported by scale licenses and certified raters • Equipped sites with clear materials and patient- facing guidelines • Minimized complexity by leveraging services within Medpace (e.g., labs, ECG, EDC) • Assigned vendor management to the study • Conducted parallel vendor start-up activities to ensure readiness by first site activation • Maintained shared documentation portals for streamlined collaboration • Performed vendor qualification, audits, and implemented quality oversight plans

• Participant retention in the context of disease progression and comorbidities • Patients experience worsening physical disability over time that may affect their ability and willingness to remain in long-term studies • Participants may become physically unable to travel to study sites or complete assessments • Emotional exhaustion may also discourage patients and their families from continuing the study	• Provided concierge services including travel and accommodation support • Enabled home assessments (e.g. spirometry, telemedicine, vocal characteristic evaluations, and home nursing service) • Determined vital status for participants lost to follow-up • Utilized composite endpoints to maximize statistical power • Ensured protocol and informed consent forms allowed flexibility around remote assessments • Simplified the study protocol by reducing unnecessary assessments • Scheduled shorter or combined visits • Enabled flexible scheduling with advanced planning and defined visit windows • Maintained consistent communication and engagement with participants and their families • Offered psychological support resources where possible and needed
• In-vivo and post-mortem tissue collection	• Enabled optional ICF for in-vivo and post-mortem optimal tissue collection, aligned with well-established local regulatory requirements • Proactively developed study-specific plans to support tissue processing steps and data transfer

LESSONS LEARNED / CONSIDERATIONS

- Neurodegenerative indications can include rare genetic and more frequent sporadic subtypes with distinct natural histories.
- Early engagement with regulators and disease communities is critical for study and protocol development, and regional submissions.
- Site and investigator selection together with community outreach and supportive programs is key to support recruitment.
- Incorporating the patients' lived experience into the schedule of assessments maximizes completeness of data collection.
- Quality by design features, detailed planning and plans, and comprehensive team trainings ensures data quality:
  - Develop a clear and detailed study protocol and use standardized procedures for all assessments to reduce variability across study sites and Investigators.
  - Provide comprehensive training for Investigators and site staff to ensure consistent and accurate data collection across sites.
  - Use validated electronic system for data entry and management and implement automated checks within EDC system to minimize transcription errors and identify data errors early.
  - Apply monitoring strategies such as centralized monitoring and remote data review to focus oversight on high-risk data and critical study endpoints.
- Multiple vendors to be proactively managed. Ensure quality oversight of external vendors to ensure consistent and validated external data. Study plan to detail responsibilities and expected oversight activities, including risks assessment.