WCG Provided Critical Support for Pediatric Rare Disease Trial, Protecting Endpoints, Ensuring Data Validity and Meeting FDA Milestones

OVERVIEW

Pediatric Gaucher disease is a devastating condition, and most patients die before they turn age 5. It is caused by a mutation in both copies of the GBA1 gene, leading to rapid, progressive and irreversible brain damage.

One sponsor is developing a gene therapy for this disease and turned to WCG for support.
The phase I/II trial is investigating a single-dose gene therapy aimed at modifying the course of Type 2 Gaucher disease in children and infants.

CHALLENGES

The sponsor faced an array of challenges, including:

- The ongoing study requires specialized expertise to monitor cognitive and adaptive functioning assessments administered by trained raters.
- Because Type 2 Gaucher is a rare disease and the patients are all very ill, finding sites and raters near the patients proved challenging.
- The trial included a complex biologic intervention. It was essential to determine if mortality and morbidity were related to the disease process itself or the gene therapy.
- The study needed to quickly make mid-course changes as the FDA provided requirements and directions.
- The study included participants who spoke different languages, adding another layer of complexity.

A great deal was at stake:
The sponsor needed to meet all the FDA requirements for this trial to be a pivotal one toward the approval of this intervention for Gaucher.

OUR SOLUTION

To address these challenges, the sponsor and the CRO turned to WCG because of WCG's demonstrated capabilities in managing complex, international studies, including those with few participants. The sponsor and CRO also needed WCG's unmatched expertise in ensuring the site raters and clinicians were highly trained – a necessity for compliance with FDA requirements.

WCG implemented several strategies, including:

Independent ratings and review

First, WCG created a three-step system to ensure the scales were being administered correctly.

01. The rater administers and rates a battery of tests that cover both the cognitive and the motor scales. This is captured on video.

02. During **central scoring**, blinded clinicians who are experts in these scales review the video and provide their own scores. The central scoring team reviews multiple administrations by site raters for verification of validity and reliability, both for the specific rater, as well as for the site and across the study

03. Finally, during **independent review,** WCG clinical scientists review the videos and the scores to confirm the rater validity, reliability and consistency in administration by the raters. If they a discrepancy is identified, WCG provides remediation rater training.

WCG also conducts a final review of the final administration for each patient who leaves the trial.

For primary caregivers, **WCG's Independent Rating** clinicians administer an adaptive function questionnaire (Vineland Adaptive Behavior Scale, Third Edition) to the child's primary caregiver. It's conducted virtually and captured on audio. WCG's participation helped ensure the reliable, professional and valid administration of a key study endpoint.

Language support

To accommodate non-English-speaking participants, WCG ensured all scales were available in the languages of all the global patients and sites.

Full WCG support

WCG also mobilized various divisions to support the study in other ways.

Analytics and statistics

The Study Insight Analytics team conducted targeted examination of data quality and collaborated with sites for improvement if necessary. WCG statistics consultants were engaged to manage complexities in data analytics.

Rater and site identification

When the needed resources were unavailable at the child's primary medical site, WCG's study acceleration team was brought in to identify appropriate raters and sites, allowing the patients to be monitored close to home.

IT support

The WCG IT support team remained available to respond effectively and quickly to site needs related to eCOA support for data capture as well as the addition of new sites.

OUTCOMES

The trial is ongoing, but to date WCG's involvement has helped:

Ensure data validity

WCG's comprehensive review process helps ensure all the data collected is accurate.

Protect endpoints

WCG experts identified rating discrepancies before they compromised signal detection.

The sponsor navigate change

WCG quickly adjusted to new requirements. Central rating, for example, was not originally included in the study design, but it was added in response to FDA queries. In fact, WCG added many services as the study has unfolded and progressed. This flexibility has helped ensure data reliability while making it easier to meet with participants and caregivers at times convenient to them.

Meet FDA requirements:

WCG promptly responded to changes in FDA requirements and directions to ensure accurate endpoint considerations. This ensured that the sponsor had the appropriate data to submit to the FDA before the deadline.

Ensure staff competency:

WCG continues to provide training and qualification through its Virgil University platform as new sites are onboarded.

To learn more about WCG services for rare disease trials, visit **wcgclinical.com.**