Synteract Helps Biotechnology Company Address Data Challenges in Coordinating Diverse Rare Disease Studies Worldwide For NDA Submission

Highlights

- Synteract has been committed to the successful NDA submission of a large mitochondrial disease program for over nine years.
- Synteract oversees safety, biostats, programming, and medical writing, and has been instrumental in addressing data challenges on the trials worldwide.
- Synteract successfully generated submission-ready datasets and tightened timelines to support accelerated submission; it continues to work with the sponsor.

Introduction

This large program of nearly 750 trials is being conducted at more than 50 clinical sites in 11 countries (USA, Brazil, Japan, China, UK, Germany, Italy, Hungary, Israel, South Africa, Australia). It includes various diseases of mitochondrial disfunction.

Challenges

Variety and size of the trials: A key challenge of the program is the diverse mix of studies and phases involved, including:

- Phases I, IIA, IIB, III
- Parent/extension
- Placebo-controlled, open label
- Sponsor-lead, partner-sponsored (Japan), physician-sponsored, NIH-sponsored
- Monitored, unmonitored
- Compassionate-use

Varying levels of diligence in data collection and cleanliness:

- For example, several did not have a CRF/clinical database, and data was instead collected in Excel.
- Some, such as compassionate-use, did not collect daily dosing data, making exposure impossible to calculate.
- Others collected only basic demographic data (i.e., no labs, ECGs, AEs), requiring Synteract to pull information from SAEs in ARGUS.

There were also a number of challenges surrounding the medication in the trial.

- While exposure/infusion data is key for analyses in this indication, it can be difficult to collect for partial/incomplete infusions.
- Summary of adverse events in relation to the treatment dose and timing are also a challenge with cross-over of subjects in the Integrated Summary of Safety (ISS and extension studies that could result in double-counting of patients under treatment and placebo groups, resulting in discrepancies between AE tables and the safety population counts.

Short timing to submission required anticipating consistency of data and requirements for analysis

- With the sponsor planning to begin work on the integration/submission by the end of the year, sufficient care must be taken to gather relevant data from all studies, as well as perform up-versioning of coding terms for AEs, concomitant medications, and so on, to create a consistent/recent version of the applicable dictionaries.

Our Solutions

Synteract oversees safety, biostats, programming, and medical writing for the over 50 clinical sites in 11 countries.

Accurate exposure and adverse event (AE) data collection is a must to enable analysis. However, with varying dose levels and multiple cycles the statistical team first needed to determine the relationship between a particular event and the closest dosing time to summarize adverse events by dose level across different cycles.

- Determining how to summarize the exposure data for their study was considered during the CRF design stage, to ensure adequate data is collected and in a manner in which it can be used.
- This also gave us a significant advantage to help shape the study analyses while thinking ahead to the submission

Synteract highly recommends that integrated CDISC-compliant datasets (both SDTM and ADaM) be created and submitted to the FDA. Although some of the older, individual studies were likely conducted prior to this requirement, the integrated datasets should be compliant to ensure a smooth review by the agency.

Results

- Despite the data challenges, Synteract has successfully generated submission-ready datasets on this large program.
- Synteract has been able to tighten timelines to support the sponsor's accelerated submission date.
- The sponsor has been pleased with the work. It has asked Synteract to perform additional tasks and support future trials.

About Synteract

With employees across 21 countries, Synteract is an innovative, full-service CRO supporting biopharma companies across all phases of drug development to help bring new medicines to market. Synteract has conducted 4,000 studies on six continents and in more than 60 countries, working with more than 26,000 investigative sites and 750,000 patients. It has contributed to more than 240 product approvals. It has conducted over 136 clinical trials in 50+ indications specifically in rare and orphan diseases in the past five years alone. In addition to rare and orphan clinical trials, Synteract offers a notable depth of therapeutic expertise in dermatology, neuro degenerative, oncology and immunotherapy, and pediatrics studies.

For more information on how we can support your clinical trial, please visit www.synteract.com/Therapeutic-Expertise/Rare-Orphan-Diseases or ContactUs@synteract.com.

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