MEDSOURCE
Taking Relationships as Seriously as Science

CASE STUDY

Sophisticated clinical trials for challenging therapeutic areas

At a time when clinical trials are becoming more and more complex – due in no small part to increased regulatory requirements – phase III trials are especially complicated, with few drugs (approximately one-third) proceeding from phase II. In such an environment, an organization seeking to conduct a trial for a rare and complicated disease state, such as life-altering central nervous system (CNS) disorders, already faces an inordinate challenge. Add further complications such as managing a small patient population, running the trial within urgent or emergency-type settings, like a hospital intensive care unit (ICU), and the difficulty-level increases manifold.

Such a case would require partnership with a clinical research organization (CRO) that could successfully undertake patient eligibility screening, conduct the trial within a limited time window due to the urgent nature of the patient's condition, and also deliver a thorough and quality data assessment to meet critical clinical end points, on time and within budget.

THE CHALLENGE

A complicated condition with limited understanding or standardized care

MedSource was selected by a clinical-stage biopharmaceutical company to create a project plan and execute all aspects of phase II and phase III clinical trials of an intravenous, inhibitory neurosteroid in the treatment of super-refractory status epilepticus (SRSE). This life-threatening, devastating neurological condition – in which a patient experiences persistent seizures, despite 24 hours or more of anesthetic treatment – is considered exceptionally rare and, to date, no standard of care or medication has been approved by the FDA, resulting in large variances in how doctors around the globe treat each patient.

The number of patients impacted by SRSE in the U.S. is approximately 1,200, so for this trial to be successful, enrolling a workable sample of patients to fit the requirements was the first significant hurdle to overcome. The urgency of treating a patient who presents to a hospital with SRSE cannot be understated; it requires a fast and effective system to be in place to, firstly, secure the subject and, secondly, to commence the trial drug, all within a very tight time frame.

Since this was the first large phase III trial for patients with SRSE, it provided a valuable opportunity to explore how best to treat these critically ill patients. To leverage the collected sample of patients, a number of additional assessments were incorporated into the trial including pharmacokinetics, central labs and EKGs at over thirty time points, an unconventional occurrence at this phase, to better understand how the drug was impacting the patient's heart as well as assessing the level of medication over a set period of time. While this added a clear benefit to the trial, it also, understandably, increased the trial's complexity.

THE STRATEGY

Securing the subjects

MedSource was successful in securing the participation of 200 hospitals based in North America and Europe, with close to 300 subjects enrolled in two years (July 2015-July 2017). Enrolling this many patients for a condition considered to be so rare was a notable milestone in and of itself and was accomplished through the efficient process established by MedSource to ensure that no patient who presented and fit the study requirements would be missed.

Up to 30 project managers, CRAs and other vital team members were available 24 hours a day and ready to be deployed at a moment's notice when a new patient was identified. Once a patient presented to one of the medical sites, MedSource would respond within the hour, via a hotline-style setup, to confirm the candidate fit the trial requirements, secure permission for enrollment, and dispense the trial drug. Because any delay in administering treatment could have dire consequences, immediate response was critical not only for the success of the trial, but to maintain the highest quality of care for these patients.

Collecting and presenting the data

MedSource worked closely with all sites to ensure the drug was administered and data was collected. The average course for each patient lasted one month. During the course of the trial, subjects were weaned off their third-line agents multiple times, necessitating that the MedSource team (all of whom had at least 15 years of clinical research expertise, as well as previous experience in ICU nursing, in many cases) train and educate each site on how to translate the weaning process into the data that needed to be recorded.

As an inpatient trial handled in an ICU setting, subjects had hundreds of pages of records to be reviewed for medical history, concomitant medications and adverse events.

MedSource initiated a process whereby complex pages regarding prior history of seizures and SRSE, along with recording the patient's timeline in the hospital and other institutions, were completed in a database.

Employing flexible and focused solutions to deliver high-quality data

Given the unprecedented nature of this program, a flexible and innovative approach was implemented to ensure high-quality data was being collected, even considering the multiple and complex additional assessments that were undertaken and the varied patient histories.

THE OUTCOME

The trial provided quality and conclusive results on time without interruption for a rare patient group where virtually no standardized care was established.

MedSource utilized an expert team to overcome the many notable challenges a complex trial such as this brings, including a rare patient group spread across continents with multiple and varied medical histories and medication plans; operating in an urgent ICU setting; and the critical need for around-the-clock support and communication with each site's hospital staff, sponsors and clinical partners.

Clear success was achieved in the delivery of a timely and definitive result to a multifaceted trial, especially when (per a widely cited study) 70 percent of all trials are delayed between one to six months. Given that a phase III trial could cost in the millions of dollars, any such delay could bring significant added expense to the sponsor company.

Reaching a clear conclusion to this particular trial, despite the statistical outcome, established a strong foundation to aid in the development of future treatments for SRSE patients and increased understanding of this rare but serious condition, its cause, and the efficacy of treatments being employed today.

VISUAL SNAPSHOT

- **Clinical trial:** Phase III trial in the treatment of super-refractory status epilepticus (SRSE)
- **Condition:** Super-refractory status epilepticus (SRSE)
- **Purpose:** To evaluate the efficacy and safety of intravenous agent in patients with SRSE
- **Patient-type:** Older than 2 years of age, suffering from SRSE, located in the U.S., Canada or Europe