Ophthalmology

Synteract Helps Complete Two Sequential, Critical Double-Masked Phase III Studies

Highlights

- Synteract was an extension of the sponsor's team in two Phase III studies.
- It came in on time, under budget on the first study and built in efficiencies on the second.
- Synteract helped the sponsor to validate the new formulation.

Introduction

Synteract prides itself on working collaboratively as an extension of our clients' teams. A study that we began working on in November 2013 is a good example of this collaboration despite business changes, delays, vacations, and weather issues.

The studies were actually two sequential, critical double-masked Phase III studies that focus on protecting, enhancing and restoring peoples' eye health. They were designed to test the next generation of a product to be used post-cataract surgery. The main goal for the first one was to test two dose regimens for an already FDA-approved product and to ascertain if a lower dosage percentage and fewer usage times per day would increase patient compliance and lower costs while still being efficacious. If so, it would help the company market the drug successfully.

The start-up phase began in November 2013. The sites were identified, Case Report Forms (CRFs) were developed and protocol was delivered. There was a five-month enrollment period planned, and despite a late start, it finished two weeks early. The study screened 612 patients to qualify 514 enrollees into the study across 45 sites. The results from this study had to be determined prior to starting the second study.

Challenges

There were a number of challenges throughout the study, including site activation delays, enrollment issues, weather, and coordinating primary investigators' (PI) vacation schedules around database closure.

The start of the study was delayed by a month because of normal contractual considerations that arose from the acquisition of the sponsor. Study start-up procedures that were already planned needed to be realigned with those of the new parent company. The process for approving sites also changed, which produced another delay in activating sites. Causing additional challenges, several storms ravaged the Midwest and Northeast, making it difficult for patients and CRAs to travel to the sites.

Another challenge was a large boost in enrollment towards the end of the trial. The projected enrollment end-date was determined based on the numbers produced over the course of the project. But after notifying the sites that enrollment was going to end, there was a sizeable jump in the screening numbers. As a result, the study was over-enrolled. This impacted the clean-up as a large amount of patient data now needed to be cleaned at the end of the trial.

Finally, site training and logistics were complex. Synteract had to set up a process to have two separate personnel on-site: one knowing and one masked. The Synteract staff had to train all the personnel in what to watch for in the event that subjects had adverse reactions to the drug. The dosage regimen required the patients to continue the medication for 18 days, a fairly long time for this type of drug, so it was important to be proactive with sites and patients to keep them compliant.

The database was scheduled to lock on July 7, 2014. Since this was right after the Independence Day holiday, the team proactively requested out-of-office schedules for both the PIs and study coordinators of all participating sites. It was apparent early in the process of gathering this data that the communication lines needed to remain open between each functional group in order to clean up the data and lock on time. Monitors and CRAs, working with project managers, had to establish priorities and move them along to complete the data before everyone started going on vacation.

Our Solutions

Synteract instituted a governance meeting involving top executives from both Synteract and the sponsor to review timelines, processes and enrollment figures. Early on, the governance committee

recognized that the study was behind on enrollment projections, so the team developed contingency plans to spur enrollment, adding more sites and allowing competitive sites to enroll up to another 25 patients beyond the original goal of 25. Although no sites signed up the full possible 50 patients—one did make it to 49—this ability spurred enrollment at those sites that had more potential and allowed the study to meet enrollment goals much more quickly.

If a site was initiated but lagging in enrollment, a CRA was sent out to the site to retrain and motivate them. All sites received either an onsite training from monitors or attendance at one of two WebEx trainings that were developed by Synteract working closely with the sponsor. A Q & A was incorporated into each WebEx session.

The team collected weekly enrollment plans from each site and compiled the information into tracking sheets that identified both planned interviews and surgery schedules. Each week, flyers were sent to the sites that outlined overall progress and gave tips on how to find patients as well as reminders on how many weeks were left until completion. This proactive communication helped to keep the sites involved.

To solve the out-of-office challenge, Synteract instituted a rolling clean-up, prioritizing the sites based on their vacation schedules and final monitoring visits. It was a demanding task for both the clinical and data management teams to ensure that all queries were resolved, diaries were submitted and investigator signature pages were collected in advance of vacation schedules.

Synteract also came up with an innovative way to solve a previous problem of spending too much time reporting data. Instead of having study coordinators or monitors fax patient diary pages into the Datafax

database system during their visits, Synteract sent each site a binder with several tabs for patient diaries to be placed after visits. During their visits, the monitors pulled the diary pages and sent them to Synteract's data entry department which in turn ran the diaries through high-speed scanners that entered information into the database very quickly. Since the data entry department bills at a lower rate than the monitors, and the process was much faster, the task became more cost-effective and efficient. This made everyone happier.

Successful Results

Overall, Synteract came in under budget with the sponsor's first study because of the efficiencies of each department and removing two weeks from the overall enrollment. The company was able to meet every study timeline and even shifted tasks forward for the benefit of the sponsor's bottom line. In addition, the flexible process for site initiation trainings had two positive results: it sped up the study timeline process and kept travel budgets lower; and in fact, web trainings were increased for the second study.

Synteract started the second study in the summer of 2014 with a twice-a-day dosage decision based on the results from the first. The team had to enroll fewer patients for the study, which also helped keep costs lower. To help the sponsor in site selection for study #2, Synteract consulted with its team of CRAs and provided the sponsor with experienced and recommended sites as a courtesy service; this wasn't part of the contracted work, but Synteract was committed to proactively supporting the sponsor to meet the study timeline.

As the second study was essentially a copy of the first, Synteract was able to build in efficiencies with the study plans and documents. They were copied and improved and drafted well in advance of the study-start. This allowed more time to focus on site activation because the team knew the timelines would be tight to get all sites activated following the finalization of the protocol. At the time of publishing, study start-up was on-track with projected enrollment.

In late 2014, the sponsor announced that the product was statistically superior to the placebo product in eliminating inflammation and pain following cataract surgery. **This Phase III study validates that the new formulation is beneficial at a lower concentration and with less frequent dosing than the current formulation.** The sponsor expects to file a New Drug Application (NDA) with the U.S. Food and Drug Administration (FDA) for the product in the second half of 2015.

> "Synteract has been an integral part of helping to support our mission of developing innovative ophthalmic pharmaceuticals. The team's skill in managing enrollment of study #1 and even coming in two weeks before the scheduled timeline—allowed us to successfully move forward with study #2. They were innovative in their approach and delivered quality services and timely results."
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> – Project Manager, Sponsor Company

About Synteract

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. Synteract offers a notable depth of expertise in oncology, general medicine, dermatology, and neuroscience indications, as well as rare and orphan, pediatric, and immunotherapy studies.

For more information on how we can support your clinical trial, please visit www.synteract.com/Services/Project-Management or ContactUs@synteract.com.

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