

Collaborative data management activities to prepare six years of data for submission

Introduction

Clinical data management (CDM) has the important role of ensuring high-quality, reliable and statistically sound clinical trial that is ready for submission. The increasing number of data sources and vendors involved in clinical trials creates challenges for efficient data management. While CDM is particularly important at the end of a study when all the data are available and need to be ready for database lock, early planning and data cleaning throughout the trial can minimize the effort at study close-out. However, this does not always occur, leaving large amounts of data to review and manage at study close-out. In these situations, a clear, well-organized plan is crucial to ensure timely database lock.

Situation

A small pharmaceutical company focusing on therapeutics to improve cardiovascular health, developed an innovative drug that was approved by the FDA as an adjunct to diet to reduce triglyceride levels in adult patients with severe (≥ 500 mg/dL) hypertriglyceridemia.

Additional data were requested from the FDA to further evaluate its efficacy and safety as “an adjunct to maximally tolerated statin therapy to reduce the risk of myocardial infarction, stroke, coronary revascularization, and unstable angina requiring hospitalization

in adult patients with elevated triglyceride (TG) levels (≥ 150 mg/dL) and established cardiovascular disease or diabetes mellitus and two or more additional risk factors for cardiovascular disease.”

In 2011, the company undertook a very large study with ~8,000 patients at 450 sites worldwide to provide the required data. Clario was subcontracted to the prime-contracted CRO to provide electronic data collection (EDC), CDM and interactive response technology (IRT) services, with integration between the Clario EDC and IRT as well as other external systems. However, although interim timelines were met, the data had not been thoroughly cleaned for the first 6 years of the study for many reasons, including challenges with communication, high turnover and the lack of a submission plan because it was unknown at the time if the study would be submitted to the FDA.

A concerted, collaborative effort was initiated in 2017 to prepare the data for final submission.

8,000
patients

450
sites

CASE STUDY

Solution

To get back on track, it was necessary to review the study documents again and reevaluate the current status to determine what needed to be addressed to prepare for database lock. For this review, the three companies held face-to-face meetings at the beginning of and again mid-year 2018.

Because of the number of patients for which data needed to be cleaned, we planned to clean them in waves (eg, in sets of 1,000 patients). First, we identified the clean data and the data that still needed to be cleaned. For the latter, we determined what needed to be completed to make that data clean. We focused on the patients with the data that needed the most cleaning first. We presented these data at the meetings, and the team worked together to brainstorm ideas about who needed to be involved and the best plan to move forward. A master spreadsheet of pending tasks was maintained, which everyone could access.

The effort included multiple teams, including those necessary for endpoint and serious adverse event (SAE) reconciliation at study close-out: safety team, endpoint team and a sub-contracted independent endpoint adjudication team.

Internally, the Clario EDC, CDM and IRT teams worked together to resolve any data integration issues and to identify the required IRT data changes to clean the data.

A follow-the-sun strategy was used to ensure timely database lock. Our global team enabled 24/7 support to resolve issues regardless of site location and time zone.

Outcomes

All of the historical data were cleaned and available for analysis by the end of 2018. The Clario IRT team processed 1,200+ of the total 7,800 data change requests during this final year of the study. In hindsight, the overall number of data changes required in the end might have been reduced if the data had been reviewed earlier, providing valuable lessons learned.

Initial results indicated positive results. Following submission and an FDA audit, the FDA approved the drug in 2019.



Systematic data cleaning process



Accessible master spreadsheet of tasks



Coordinated effort across teams



EDC, CDM and IRT involvement



Follow-the-sun strategy

Visit clario.com to learn more about our EDC, CDM and IRT solutions.