CASE STUDY

Bioclinica Cardiac Safety Services Offered an Effective Answer for a Specific Regulatory Requirement

Introduction

To ensure patient safety, outcomes related to cardiac safety are important for drug development across all therapeutic areas. As such, measurements related to QT interval prolongation and proarrhythmic risk are mandated by regulatory authorities. Furthermore, monitoring of off-target effects on cardiac function with some drugs (e.g., oncological and neurological drugs, among others) might be required for submission. Particularly in these situations when the equipment and expertise to monitor cardiac function might not be available in specialized clinics, cardiac safety services can prove useful. They traditionally include standardized capture and transmission of ECG and blood pressure data, as primary safety assessments, to the core lab for analysis by board-certified cardiologists.

Situation

The client is a small biopharmaceutical company that focuses on therapeutics in immune disorders. During the development of an oral therapy to treat relapsing multiple sclerosis, an off-target effect of bradycardia occurring up to 6 hours after the dose was identified. Therefore, as part of the regulatory requirements for the Phase 2/3 trial evaluating the efficacy and safety of the drug, heart rate (HR) needed to be monitored via ECG by a centralized lab for a minimum 6 hours after the dose. Only if HR had normalized at the 6-hour timepoint could the patient be discharged from the neurology clinic.

To ensure patient safety and expedite discharge (avoiding a prolonged stay in the neurology clinic), the client required the 6-hour post-dose HR information from the ECG within a 3-hour turnaround time.

In response to the client's RFP and as part of the bidding process, members of Bioclinica's medical/scientific, project management and business development teams had ongoing meetings and consistent follow-up with the client to discuss potential solutions. These solutions were developed by Bioclinica specifically for the client's needs, study-specific requirements and regulatory requirements. This solution-focused approach included implementing and coordinating resources across Bioclinica's global offices (e.g., the US and China).

PHASE 2/3

Part A
Multicenter
Randomized
Double-blind
Placebo-controlled

Part B
Double-blind
Double-dummy
Active-controlled
Parallel group study

~5
YEARS
(9/12 – 5/17)

180
SITES

21
COUNTRIES

>2000
SUBJECTS

Solution

After becoming the chosen outsourcing partner, Bioclinica worked closely with the client to continue developing and refining the unique service solution involving medical, project management and technology-based perspectives and to meet the specific request from the regulatory authorities, the needs of the clinical sites and the overall development plan of the compound. Multiple perspectives were used, including medical, project management and technology-based.

The cardiovascular safety endpoints were 12-lead ECG and 12-lead digital Holter as well as a 3-hour initial ECG overread based on ECG and HR threshold criteria. Pre-dose and 6-hour post-dose ECG readings were required to meet the clinic discharge criteria. In addition, during part A of the study (double-blind, placebo-controlled), 12-lead digital Holter measurements for 75 patients were used to monitor HR response.

The initial solution required partnership with a Holter/ECG technology company. Through a very interactive process, Bioclinica and the device company created a bedside solution to monitor HR trends. The sites would have been able to view the HR activity onscreen, store ECG data for the full monitoring duration and generate specific ECG tracings at the protocol pre-defined time points. However, based on continued discussions with regulators, this solution was deemed unnecessary, and expedited central overread of the specific ECG timepoints prior to patient discharge was sufficient. Therefore, Bioclinica provided this service.

To train the study team, five investigator meetings were held, with 5-10 breakout sessions per meeting. A two-step process was employed, with a member of the cardiac tech team performing the initial read and the study-specific US-board certified cardiologist performing the final read. A "follow-the-sun" on-call system was established to ensure timely readings of the 6-hour post-dose ECG in each time zone, which was a key component to allowing the patient to leave the clinic.

OUTCOMES

13,505
12-LEAD ECGS OVERREAD

4,000
EXPEDITED 3-HOUR INITIAL ECG READS

"I have worked with the project manager on several of our supporting clinical pharmacology studies. No two were exactly alike – each one presented unique challenges, and she greeted each challenge as an opportunity to solidify the partnership between our two companies."

– Senior Manager Clinical Trials

Outcomes

The collaborative working relationship between the client and Bioclinica enabled an effective solution that met the client's needs over the course of the 5-year study. Internal resources were adapted to address the requirements of verifying patient safety and allowing the patients to leave the clinic in a timely manner. The study was completed on schedule, and the majority of the expedited ECG overreads were completed within an hour or less, much shorter than the contracted 3-hour turnaround time. The Bioclinica global network of offices enabled this quick turnaround time regardless of patient location. The client viewed Bioclinica as a partner in the development efforts, rather than as a core lab vendor, and Bioclinica and the client continue to have a long-standing relationship, including the same core team.

Summary

The client was able to tap into the resources of a trusted research partner with whom they had worked previously to develop a global solution for a unique requirement. As a result, regulatory requirements and expectations were met with regards to safety outcomes.