CASE STUDY

Clario helps establish the cardiac safety profile of a novel oncologic in early phase

Cardiac and oncology expertise leveraged to drive successful outcome in global trial

The challenge

Cancer drugs can often be toxic with resulting cardiac safety side effects. However, establishing the cardiac risk of such drugs in development faces many challenges as patients are often very ill with numerous complicating factors, age-related comorbidities and concurrent medications, some with a known cardiac safety impact. This can result in:

- High data variability
- Inconsistent ECG data analysis
- Imprecise reader measurements

The inherent toxicity of chemotherapeutics prohibits the ethical, safe use of traditional cardiac safety assessment methods, such as placebo trial arms, healthy volunteer studies and supratherapeutic doses. Without such measures, effectively establishing cardiac risk is particularly challenging, and the data that can be collected need to be of the highest quality. Therefore, having a disciplined development strategy with a partner experienced in minimizing data variability in oncology trials is critical to prevent prohibitive labels from regulators.

Situation

A pharmaceutical company conducted a Phase I/II study for solid tumors across 40 sites in the U.S. and Europe. The potential impact of the investigational drug on cardiac safety needed to be assessed. During site visits, periodic ECGs and blood samples were collected from patients over an 8-hour period.

To enable concentration-QTc (C-QTc) analysis, Clario was engaged to collect and centrally measure triplicate 12-lead ECGs that were time-matched to the blood samples that were taken for pharmacokinetic (PK) assessment.

Summary

- Phase I/II study for solid tumors across 40 sites in the U.S. and Europe
- Assessment of cardiac safety, including ECGs and blood samples for PK assessment
- Data collection strategy and execution directed by Clario's cardiac experts
- Retrospective ECG extraction, measurement and interpretation of C-QTc analysis
- Findings accepted by the FDA, enabling a favorable label for the sponsor

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Clario solution

The Clario approach involved full consultancy services as well as ECG data collection and analysis, including:

- Direction by Clario's experts regarding cardiac data collection methodology and timing, appropriate sample size, statistical analysis and more
- Development of the EXPERT report, data sets and xmls of ECG waveforms in formats to meet regulatory requirements
- Provisioning of resting 12-lead ECGs and 12-lead Holter devices
- Device training for the sites
- Safety ECG overread by Clario's central core lab
- Prospective arrhythmia analysis from 12-lead Holter data
- Retrospective ECG extraction, measurement and interpretation of C-QTc analysis

Impact

Reliable data

- Successfully established QT risk in a complicated population despite the significant challenges inherent in oncology trials

Cost savings

- Early-phase analysis that prevented the need for a more robust and costly QT study

Regulatory acceptance of findings

- Acceptance of the findings by the FDA, enabling a favorable label for the sponsor

Clario's success factors

Clario's solution was successful based on the following factors:

Experts in cardiology and oncology

- Advice on study design, data modelling and analysis
- Data collection strategy that considered potential complications and involved highly precise ECG overreads to minimize data variability
- Data analysis and presentation of the findings for FDA submission

Site training

- Training of sites on new resting 12-lead ECG and 12-lead Holter devices
- Assurance of high-quality ECGs

Experienced central core lab

- Interpretation of ECGs by readers with oncology indication experience
- Standardized methodology for ECG interpretation

Retrospective analysis of standardized ECGs

- Use of previously acquired Holter data for C-QTc assessment
- Statistical analysis and EXPERT report

Our team of experts is ready for your questions about monitoring cardiac safety in your next oncology clinical trial. To contact us, go to clario.com/solutions/cardiac-safety or email info@clario.com.

Clario is a leading provider of endpoint data solutions to the clinical trials industry, generating high-quality clinical evidence for life sciences companies. We offer comprehensive evidence-generation solutions that combine medical imaging, eCOA, precision motion, cardiac and respiratory endpoints.