A Heart-Pounding Development in QT Assessment

January 6, 2015 ***Lorraine Rusch***

On Friday, December 12, 2014, the news of a technique for reliably assessing QT/QTc from data captured during routinely conducted Phase I studies was shared during an FDA-hosted Cardiac Safety Research Consortium meeting with attendees from the regulatory, biopharma and medical communities.

As announced in the Wall Street Journal article on December 18th, "iCardiac Technologies, Inc., a provider of cardiac safety assessment services, in the fall completed a study in collaboration with the U.S. Food and Drug Administration that demonstrated cardiac toxicity in drugs can be detected much earlier in the development process than previously thought by medical professionals."

Over the last decade, QTc studies have been conducted for almost all New Chemical Entities (NCEs) exhibiting systemic exposure. At a cost of approximately $2 to 4 million per study, TQT represents a significant investment and development risk considering a positive finding can result in onerous late-stage or post-approval commitments for safety monitoring. It can also completely end the development of the compound.

The Cardiac Safety Research Consortium-FDA study demonstrated that the new cardiac technology allows this assessment to be conducted as early as during the First-in-Human (FIH) dosing study. These studies are typically administered to healthy normal volunteers in single doses to small cohorts in an ascending manner with the objectives of evaluating safety, tolerability, pharmacokinetics and potential dosing regimen for further studies in Patient populations.

Newer and more rigorous modeling techniques are being utilized to maximize the power of smaller sized studies with increased data collection and analysis. The methodology includes a significant increase in ECG data evaluation, use of improved algorithms for cardiac assessment and careful analysis of compound systemic exposure to create a powerful combination of maximal data points in a smaller clinical trial performed as part of a required FIH study.

The question of the FDA acceptance of this new paradigm was addressed frankly by Dr. Norman Stockbridge, a director in the Division of Cardiovascular and Renal Products at the FDA's Center for Drug Evaluation and Research. Dr Stockbridge stated to the Wall Street Journal that "if a pharmaceutical company comes to me with results using this type of a methodology, and the study is well conducted with high quality electrocardiogram data collection and analysis, I'm ready to recommend its use in regulatory decision making today."

This clear pathway forward is indeed a revolutionary attitude, freeing pharmaceutical companies to evaluate their potential therapies earlier in development, provide more product valuation for companies looking for further investment or partnering, and most importantly create an early translation of preclinical cardiac safety studies into viable human data and a safety platform for further clinical trials.