



UNIVERSITY *of* ROCHESTER

Academic Perspectives

Computerized QT measurements and Repolarization Morphology

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CSRC/HESI Session: Pre-clinical and clinical testing for QT proarrhythmia: how do they related to one another and to risk of life-threatening arrhythmic events?

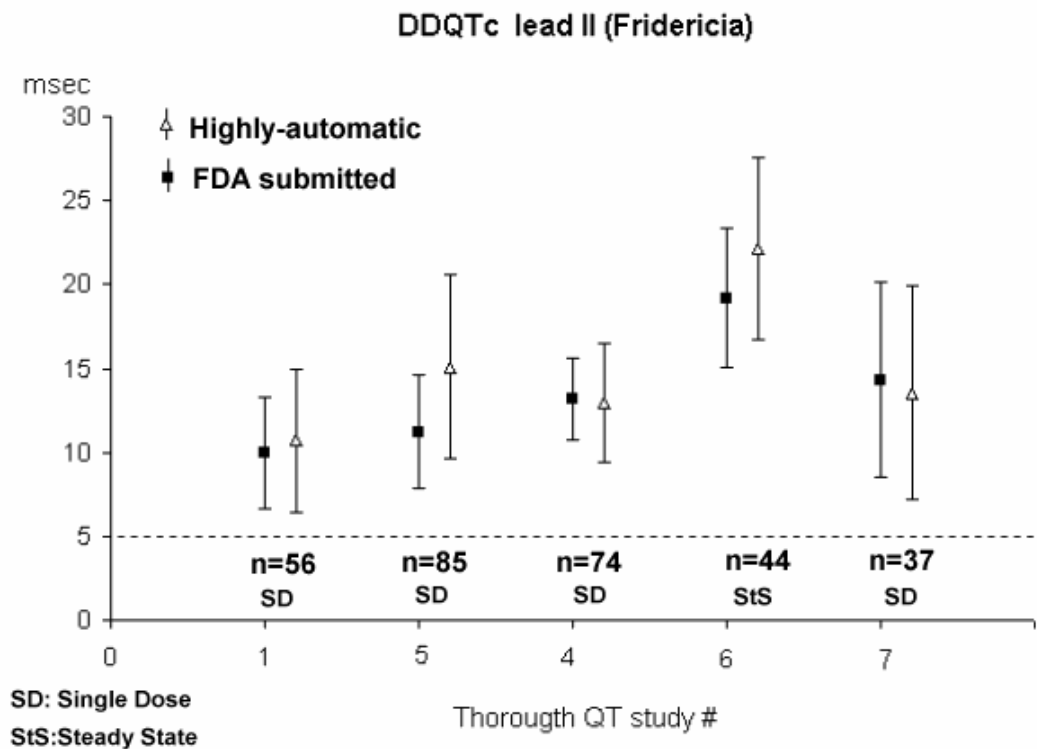


“.. manual and automated commercially available QT algorithms demonstrated small statistically significant effects on the QTc interval induced by positive controls ..” *

Computerized vs. FDA-submitted QTc Prolongation at PK
(3,595 ECGs from 296 individuals enrolled in five thorough QT studies)

50 ECGs were adjusted (1.4%)
20 ECGs were not in sinus rhythm (0.6%)

(JP. Couderc, C. Garnett, M. Li et al. NIH R01 #HL084402-01 - Unpublished data).

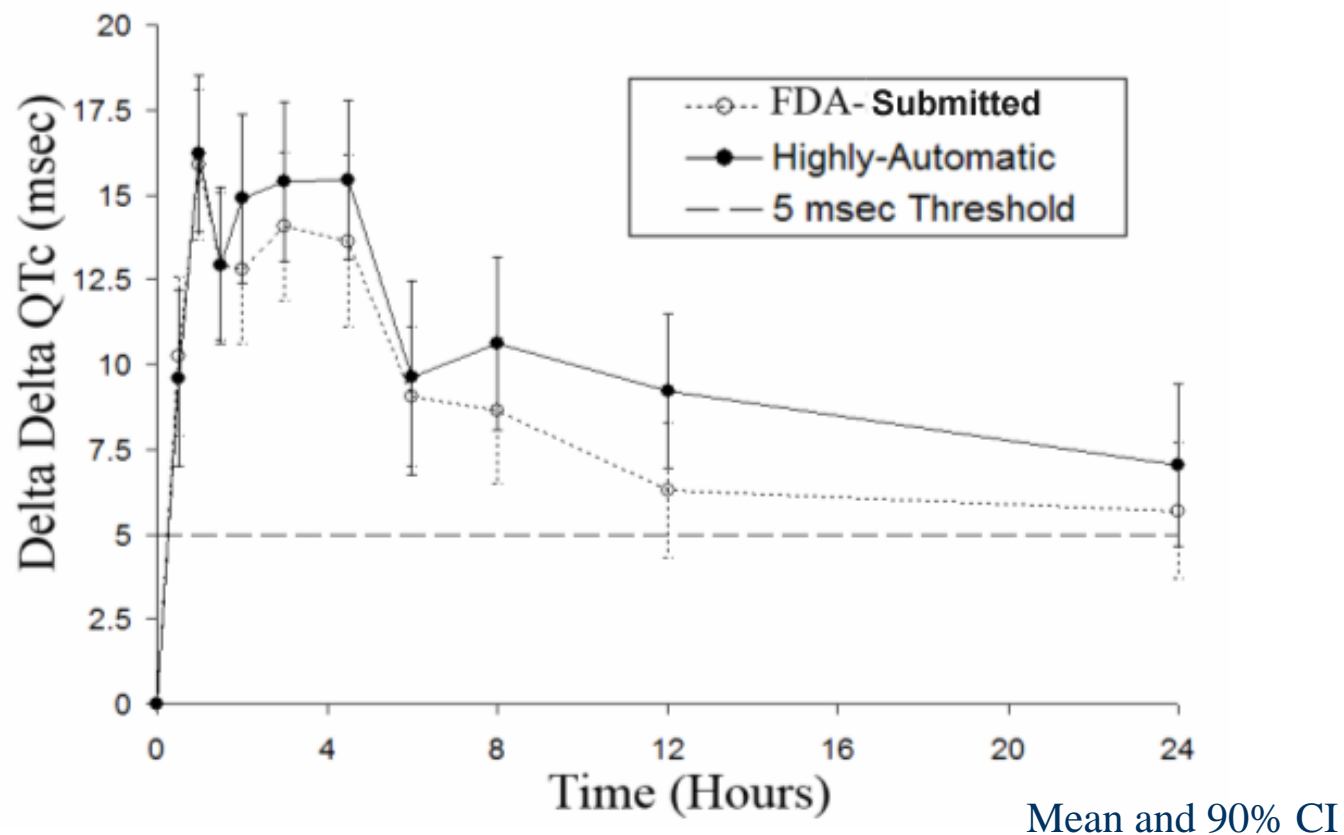


Mean and 90% CI

* Darpo B, Agin M, Kazierad D, et al. Man Versus Machine: Is There an Optimal Method for QT Measurements in Thorough QT Studies?. J Clin Pharmacol. 2006;46:508-612



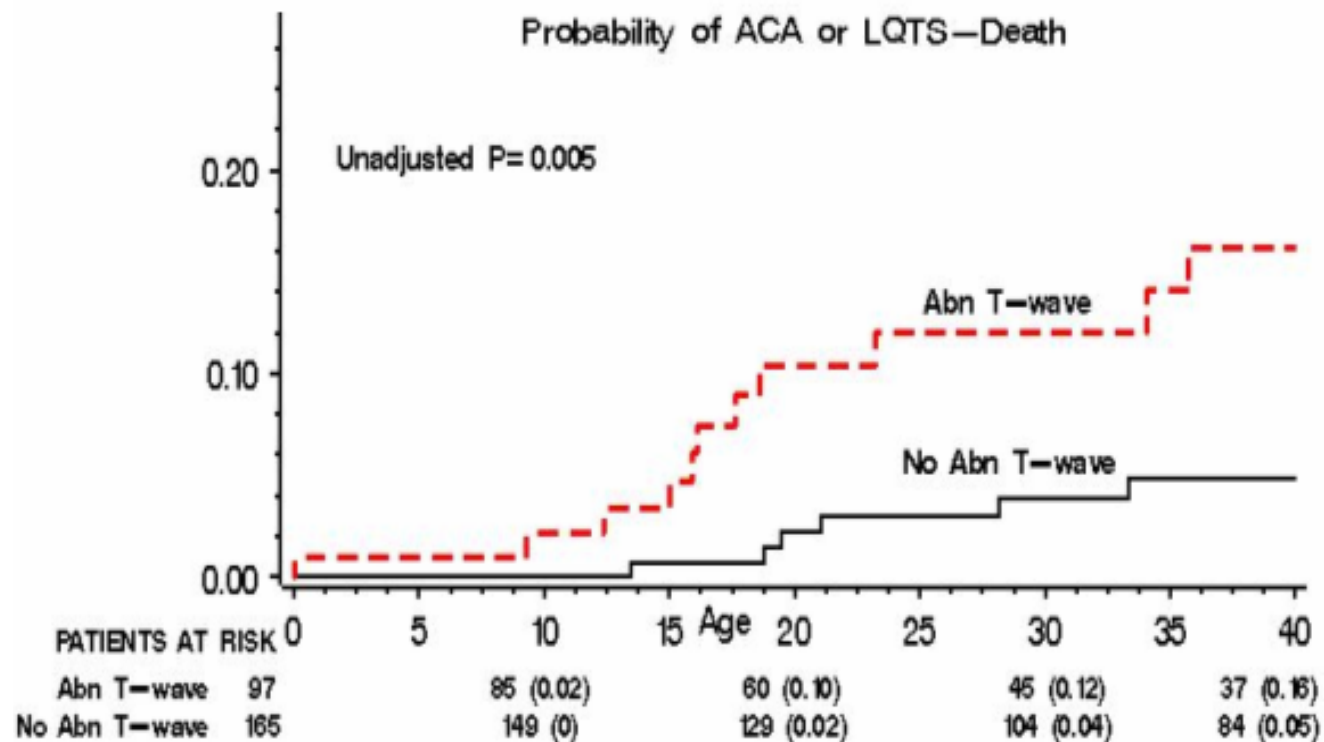
Moxifloxacin-Induced QTc Prolongation Profile (Highly-automatic vs. FDA-submitted) (8,911 ECGs from 66 individuals, all females)



* R. Handzel, C. Garnett, et al. Comparison between highly-automatic vs. FDA-submitted QT measurements for the detection of moxifloxacin induced prolongation of the QTc interval. *IEEE Comp. Cardiol.* 2008 (in press) ³

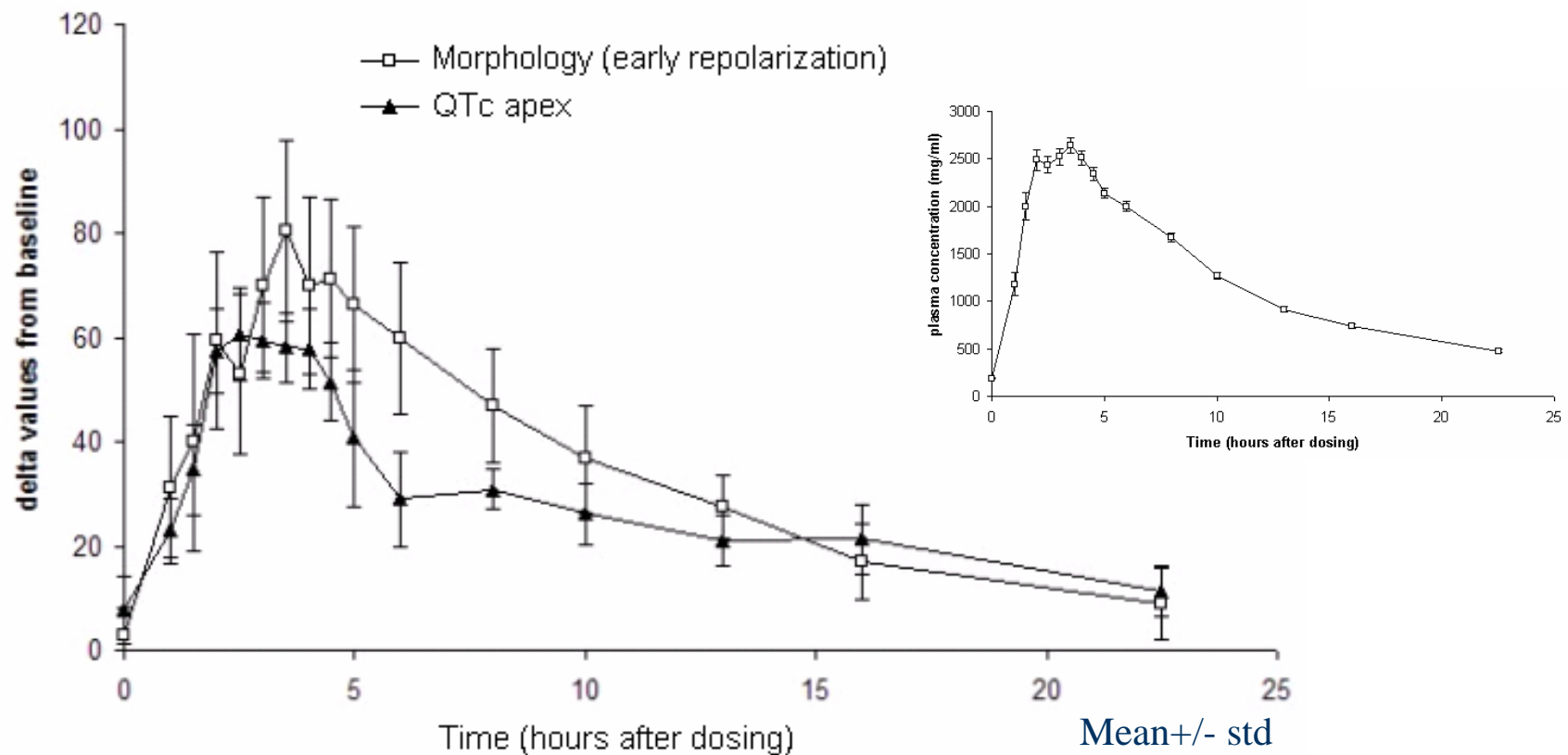


Abnormal T wave morphology and Aborted Cardiac Arrest or Death in LQT2 Patients with QTc between 440-500 ms





Sotalol-induced repolarization heterogeneity and QTc apex prolongation are dissociated.





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TELEMETRIC and HOLTER ECG Warehouse

THEW-project.org



FDA and University of Rochester Partnership

- Facilitate collaborative discussions, leveraging of resources for the implementation of joint projects among FDA, UR, and other public and private stakeholders;
- Develop, identify and evaluate new electrocardiographic markers of cardiovascular risk related to management of patient care and evaluation of new molecular entities;
- As appropriate, incorporate scientific findings from the THEW into the pre-market evaluation process for ambulatory electrocardiographic devices, and into the total product life cycle.