Electrocardiographic Changes Associated with Ibrutinib Use

Michael G. Fradley[1,2], Josephine N. Emole[1], Federico Viganego[1,2], Matthew B. Schabath[1], Bijal D. Shah[1], Julio C. Chavez[1], Christine M. Walko[1], Howard L. McLeod[1] and Javier Pinilla-Ibarz[1].

[1]H. Lee Moffitt Cancer Center and Research Institute
[2]University of South Florida, Morsani College of Medicine

Character Count: 1965

Presenting Author Contact Information:
Michael G. Fradley, MD
2 Tampa General Circle, 5th Floor
Tampa, Florida 33606
mfradley@health.usf.edu
Phone: 203-887-4544
Fax: 813-745-7255

Background: Although ibrutinib-associated supraventricular tachycardia (SVT) and atrial fibrillation (AF) have been well described, there is little information about ibrutinib's effects on other electrocardiographic or electrophysiologic parameters, particularly in a "real-world" population. In our retrospective study, we evaluated the changes on the surface electrocardiogram (ECG) of patient's exposed to ibrutinib, outside of a clinical trial.

Methods: We analyzed data on 73 patients treated at Moffitt Cancer Center between 11/13/13 and 3/31/15 who completed at least one 28-cycle of ibrutinib. Among the 48 patients in this cohort with a documented surface ECG, there were 12 patients in whom an ECG was obtained both prior to- and after ibrutinib exposure. The signed rank test was used to evaluate for any statistically significant changes in commonly measured electrocardiographic variables including rate, ventricular axis, PR interval, QRS duration and QT interval.

Results: In the total study cohort, the incidence of AF (or other SVT) was 12% (n=9). Indications for ibrutinib were primarily chronic lymphocytic leukemia (71%) and mantle cell lymphoma (22%). Comparing ECGs pre- and post-ibrutinib exposure, there were no statistically significant differences in the measured parameters with the exception of the absolute QT interval which was generally shorter after exposure to the drug. The median pre-QT interval was 384ms compared to a median post-QT interval of 367ms (p=0.045). There were no significant differences in the corrected QT intervals using either the Bazett (p=0.388) or Fridericia (p=0.126) formulae however.

Conclusions: Although we observed QT interval shortening after ibrutinib exposure, other common ECG intervals were not significantly changed. In addition, the incidence of AF in our study was higher than that reported in the original clinical trials. The way in which ibrutinib exerts its arrhythmic effects remains uncertain, however the findings in this study may point to a common underlying electrophysiologic mechanism, such as action potential duration shortening. These data may help in developing future basic science studies to further understand the cardiotoxicity of ibrutinib.